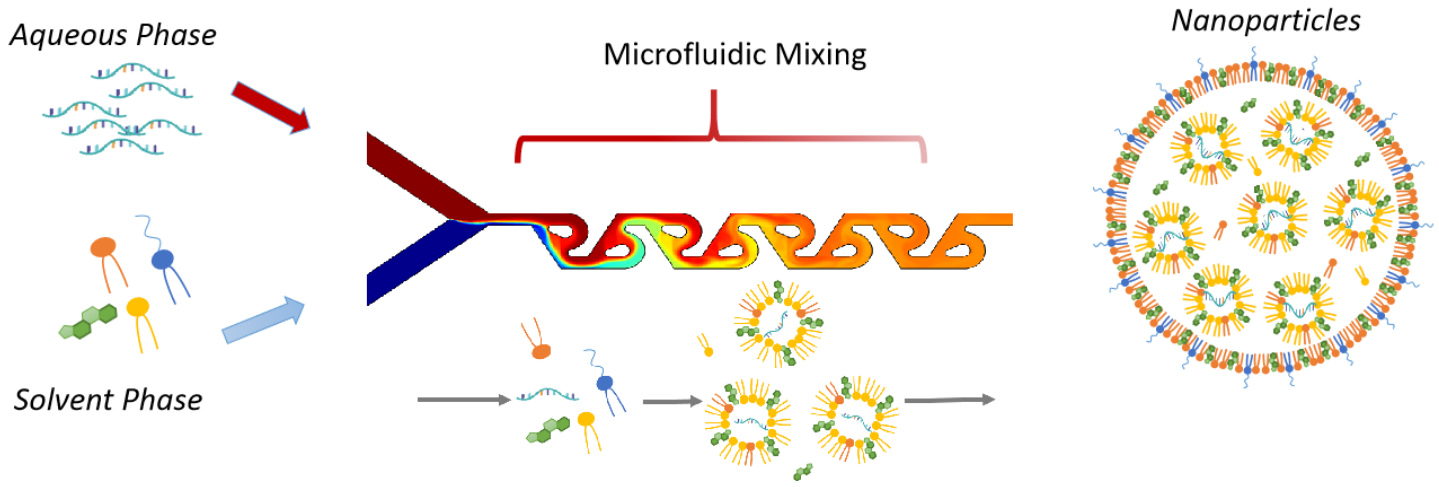
NanoGenerator® Nanoparticle Synthesis System and LipidFlex™ Formulation

PreciGenome

Sep 2024

What is Lipid Nanoparticle?

Lipid nanoparticles (LNP) are self-assembling structures of natural or synthetic lipids in aqueous environment.

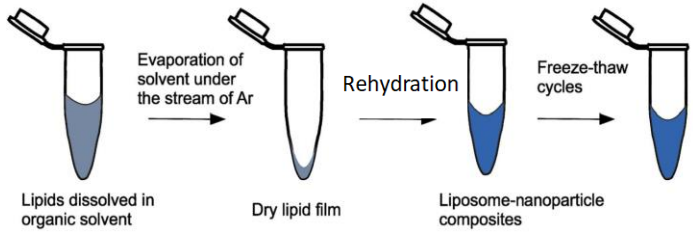


- Cationic/ionizable lipid
- Structural lipid
- Cholesterol
- PEGylated lipid
- Nucleic acid payload

Lipid Nanoparticle Synthesis Methods

Conventional Methods

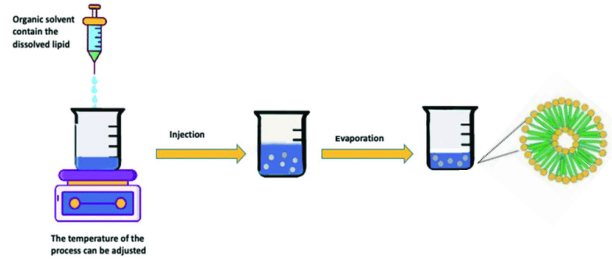
A Film hydration



- Established method
- Understood method

- High consuming of the organic solvent
- High PDI
- Lack of reproducibility
- Need for additional downsizing step
- Difficulties in scaling-up

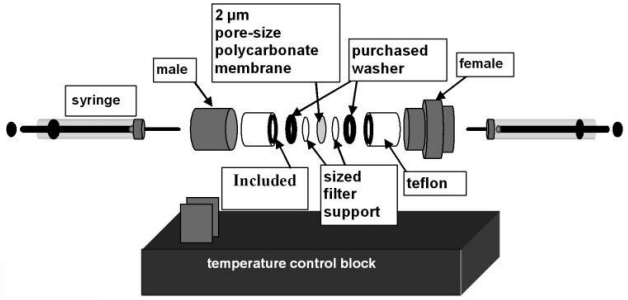
B Solvent injection



- Simple and fast
- Scaling-up possibility

- Exposing to organic solvent
- High PDI
- Stability problem

C Extrusion



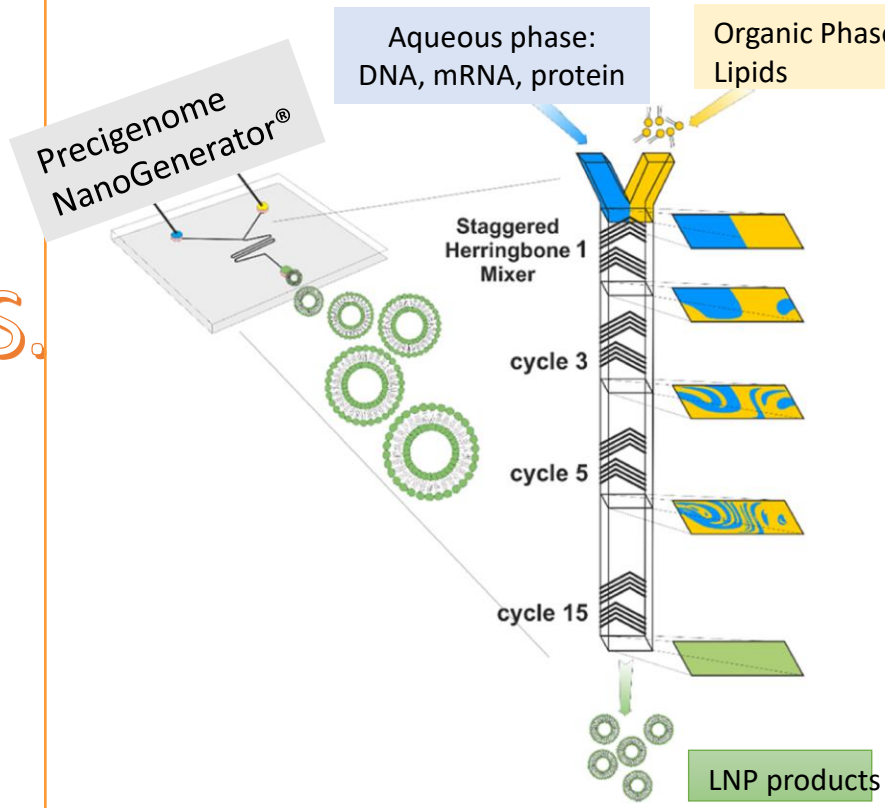
- Uniform and homogenous formulation

- Possible clogging of the membrane pores
- Difficulties in scaling up

Nanomaterials, Volume 11, 2021, 3440

VS.

Microfluidic Mixer



Reference: Scientific Reports volume 10, Article number: 5595 (2020)

NanoGenerator® - Nanoparticle Synthesis System

Discovery & Screen

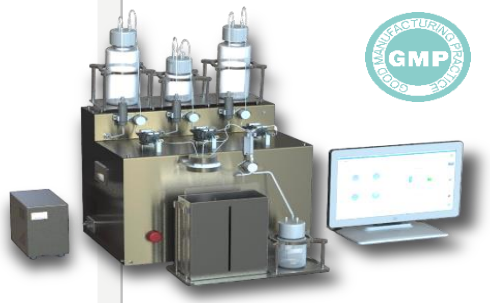
Pre-Clinical

Clinical

Commercial

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

Flex-M
1 – 12 mL per run
Flex-M Premium
1 – 75 mL per run

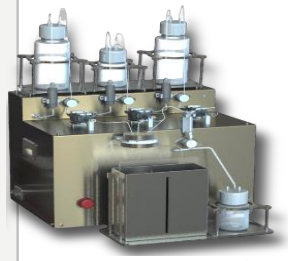


MAX (cGMP)
50 mL – 1 L per run

MAX+ (cGMP)
>20 L per run

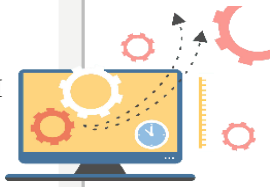
PRO
2 – 200 mL per run

Flex-S Plus
0.1 – 0.5 mL per sample
1 – 32 samples/run
Up to 96 samples/hour



MAX (RUO)
50 mL – 1 L per run

Custom design and OEM solutions



>20 L throughput

Target Validation
API Identification
Excipient Identification

Formulation Development & Optimization
Candidate Selection

Clinical Development
Approved Medicine
Customized GMP Solution





BASIC FEATURES	Flex-S	Flex-M	Flex-M Premium	PRO	MAX	MAX (40L/H)
Product Model Number	PG-SYN-FS	PG-SYN-FM	PG-SYN-FM	PG-SYN-P	PG-SYN-G	PG-SYN-G
R&D Stage	Screening & Discovery	Screening & Discovery	Screening & Discovery	Preclinical Studies & Development	Preclinical Studies & Development	Clinical Development & Production
Throughput	0.1 to 2 ml	1 to 12 ml	1 to 75 ml	2 to 200 ml	50 ml to 1 L	>20L
Multiple Samples Per Run	✓	✗	✗	✗	✗	✗
Max Flow Rate	3 or 4 ml/min	5 ml/min	24mL/min	24 ml/min	4.8 L/h	40L/h
Flow Rate Ratio	3:1	1:1 to 5:1	1:1 to 10:1	1:1 to 5:1	1:1 to 9:1	1:1 to 5:1
Tunable Flow Rate	✓	✓	✓	✓	✓	✓
Intuitive & Easy To Use	✓	✓	✓	✓	✓	✓
Compact Design	✓	✓	✓	✓	✓	✓
Consumable Cost Per Run	$	$	$	$	$$	$$$
Dimensions	32×40×21 cm	53×27×24 cm	53×27×24 cm	38×40×36 cm	62×38×43 cm	62×38×43 cm
Weight	8.1 kg	10.7 kg	10.7 kg	16.1 kg	50 kg	65 kg

Scalable LNP Production

NanoGenerator®
Flex-S/Flex-S Plus

Early
Screening

0.1 – 2 ml

NanoGenerator®
Flex-M/Flex-M Premium

Small Production

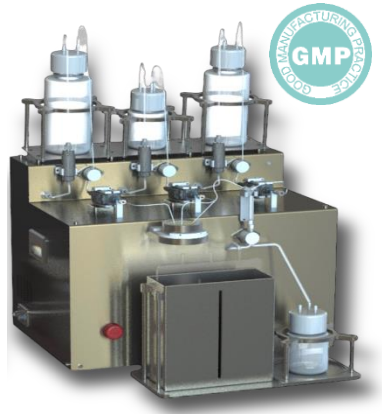
1 – 12 ml (Flex-M)
1 – 75ml (Flex-M premium)

NanoGenerator® Pro

Medium
Production

2 – 200 ml

NanoGenerator® Max



Commercial Production

50 ml – 1 L (MAX);
> 20 L (MAX 40L/H)

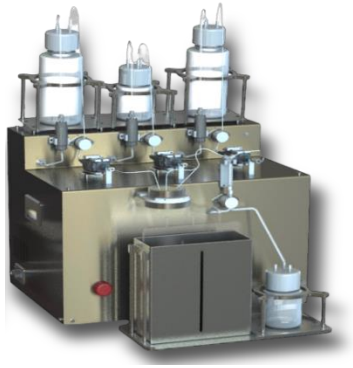
NanoGenerator® Scaling Up

- Transferable results from early screening (Flex-S, 0.1mL) to pre-clinical development (Pro, 200mL), then commercial production (Max: 1L, MAX 40L/H: >20L)

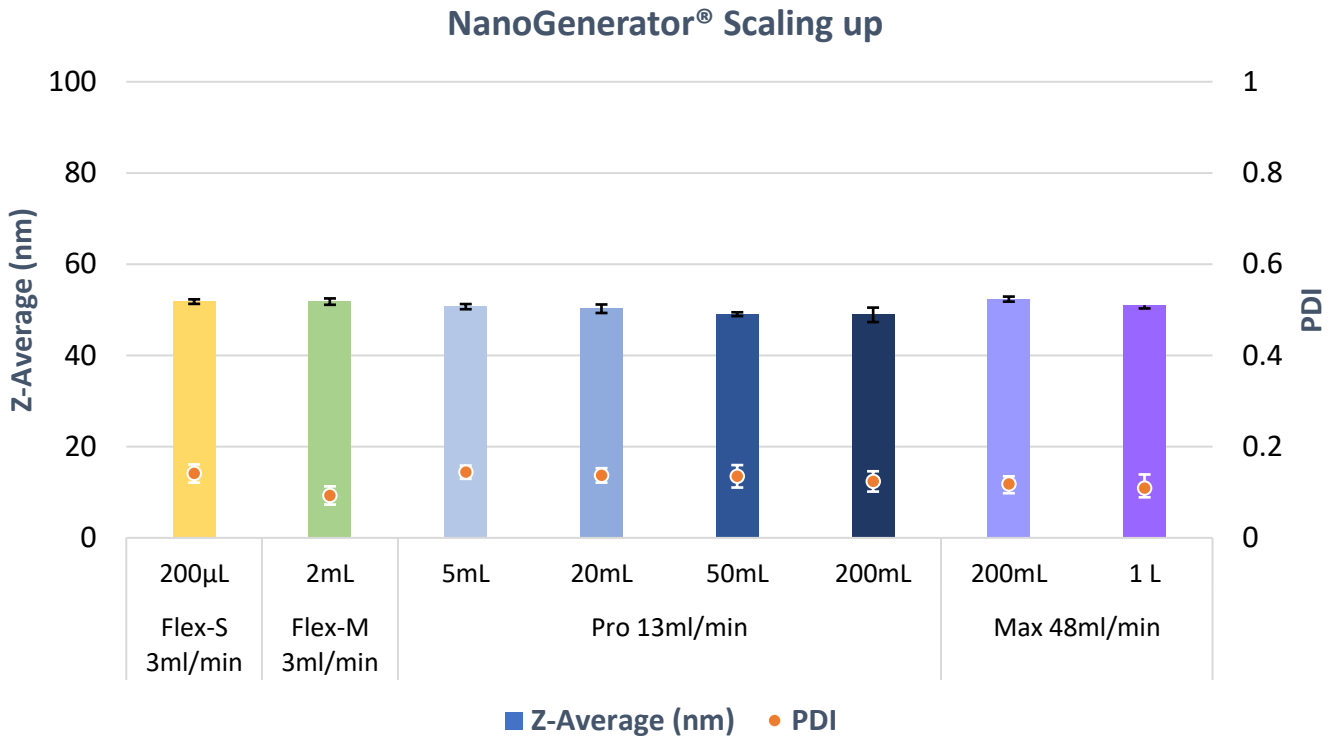
Flex-S: 0.1 – 2 ml

Flex-M: 1 – 12 ml
Flex-M Premium: 1 – 75ml

Pro: 2 – 200 ml

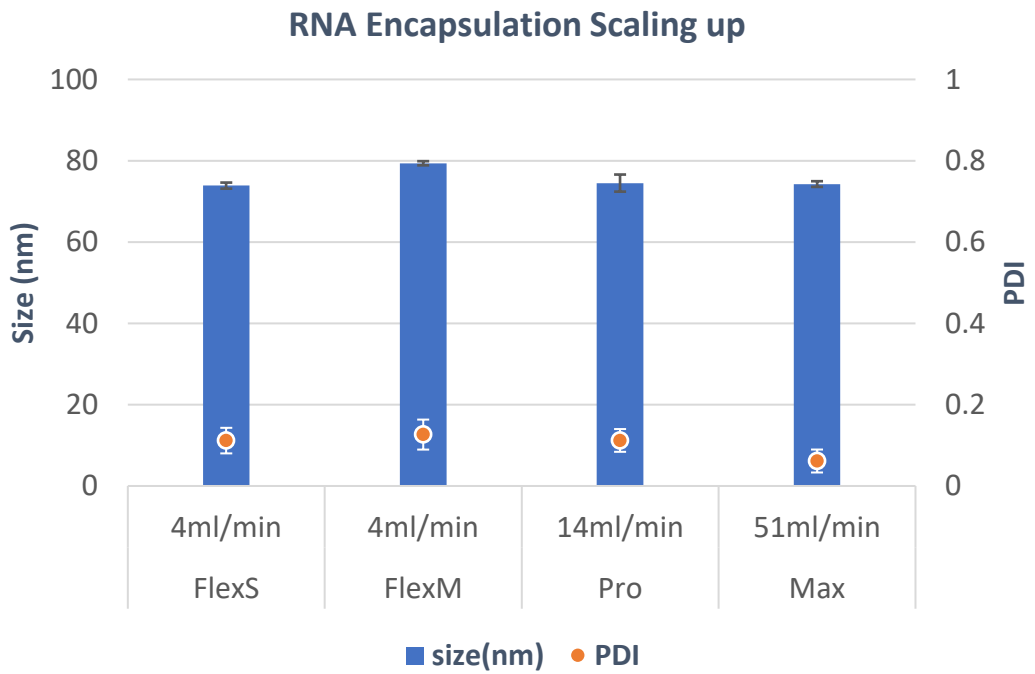


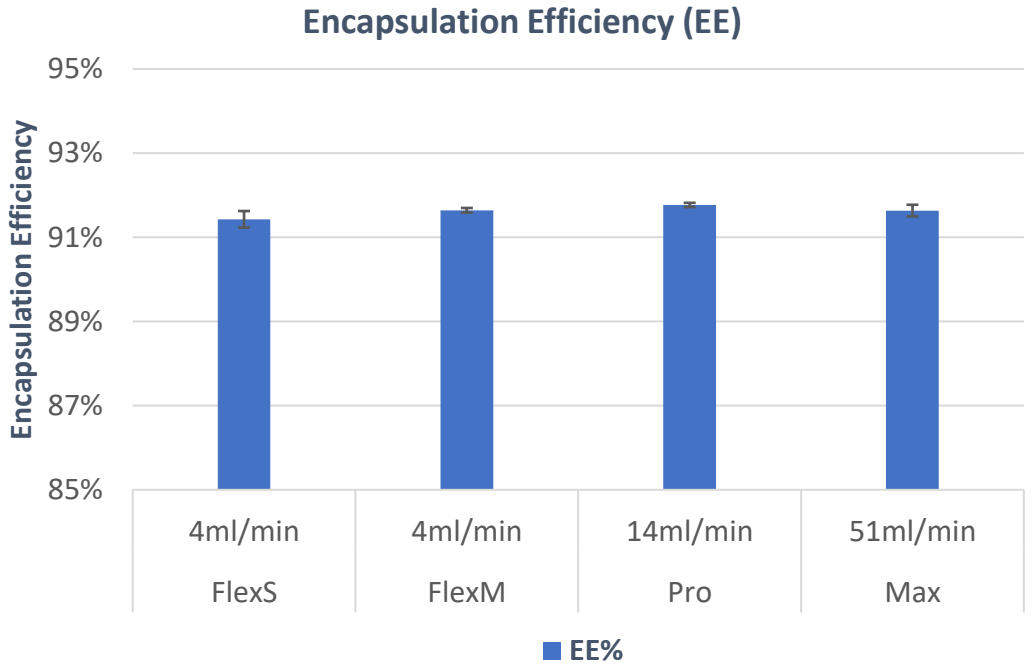
MAX : 50ml – 1L
MAX (40L/H): >20L



Reagents	
Aqueous phase	Sodium acetate buffer (100mM, pH5.2)
Solvent phase	LipidFlex, 15mM in ethanol

NanoGenerator® — Scale Up





	Reagents
Aqueous phase	Sodium acetate buffer (100mM, pH5.2)
Payload	RNA (~600 nt)
Solvent phase	LipidFlex RNA-LNP kit

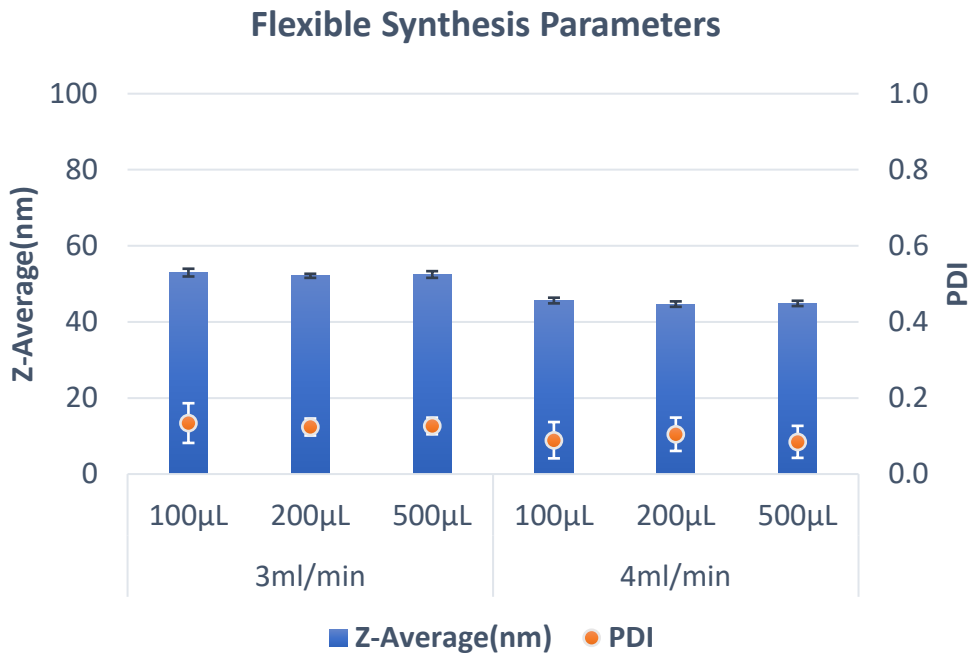
NanoGenerator® Flex-S

- 0.1 – 2mL synthesis volume per batch
- Tunable total flow rate (3ml/min & 4ml/min)
- Customized total flow rate & flow rate ratio available
- Multiple sample synthesis per run available
- Disposable consumables

NanoGenerator® Flex-S

	NanoGenerator Flex-S	Syringe Pump Systems	Tubing Connection Systems
Dead volume per sample	< 20 µl	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	0.1 – 0.5 mL	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

NanoGenerator® Flex-S

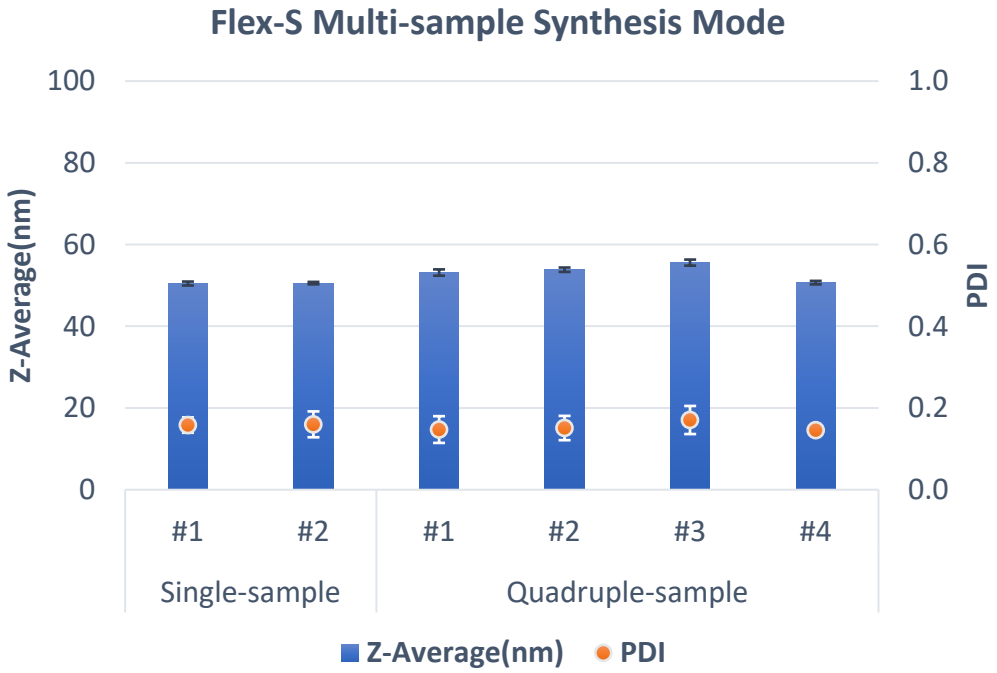


Model	Flex-S
Aqueous phase	Sodium acetate buffer, 100mM, pH5.2
Solvent phase	Lipidflex, 15mM in ethanol

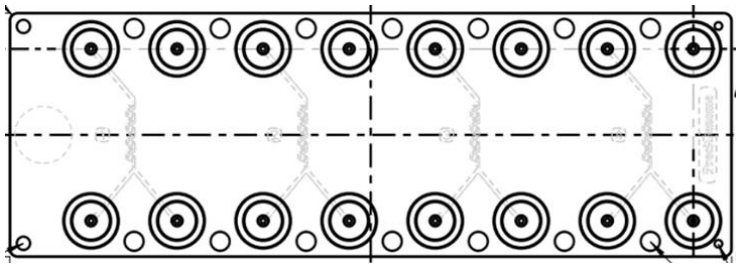
NanoGenerator® Flex-S

- **More total flow rate setting options.**
  - Users can choose **3ml/min** or **4ml/min** to conduct LNP synthesis.
  - Higher flow rate setting generates LNPs of smaller particle size.
- **Low synthesis volume limit (100 – 500 μL) per sample**
  - Minimum aqueous sample input volume: 75 μL
  - Minimum Lipid formulation input volume: 25 μL
- **Excellent batch-to-batch consistency**

NanoGenerator® Flex-S



Model	Flex-S
Aqueous phase	Sodium acetate buffer, 100mM, pH5.2
Solvent phase	Lipidflex, 15mM in ethanol



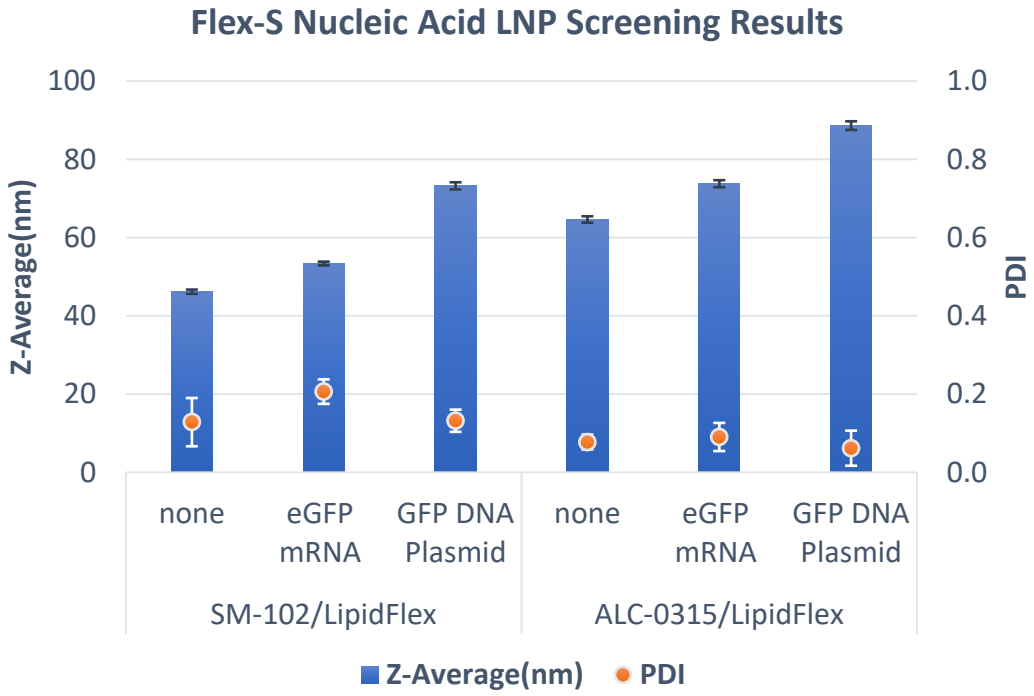
CHP-MIX-4

Multi-sample Synthesis by NanoGenerator® Flex-S:

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

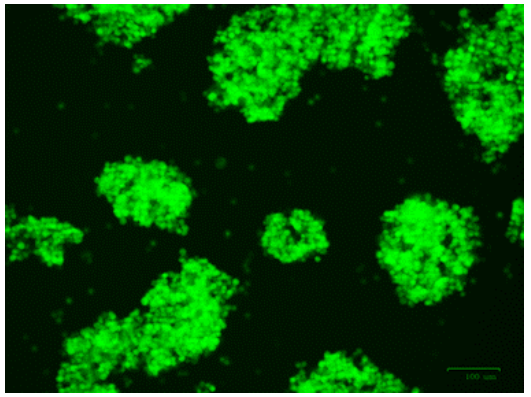
- **Reliable screening results.** Using PreciGenome's advanced air-flow control technology, users can obtain reliable LNP results on both single- or multi-sample synthesis modes.

NanoGenerator® Flex-S



Model	Flex-S
Aqueous phase	100 µg/mL eGFP mRNA (CATUG) or GFP DNA (ALDEVRON) in sodium acetate buffer (100mM, pH5.2)
Solvent phase	Ionizable lipid/Lipidflex, 40/60, 12.5mM in ethanol

eGFP mRNA LNP Delivery to Jurkat Cells



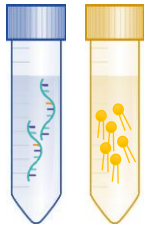
Jurkat Cells transfected with eGFP mRNA LNP. Green fluorescence image at 48 hours post transfection.

- **Robust Formulation Screening.**
  Using NanoGenerator® Flex-S, users can conduct formulation screening using minimum reagent consumption, which saves lots of cost.

- LNP size and PDI depend on the payload and formulation choice.

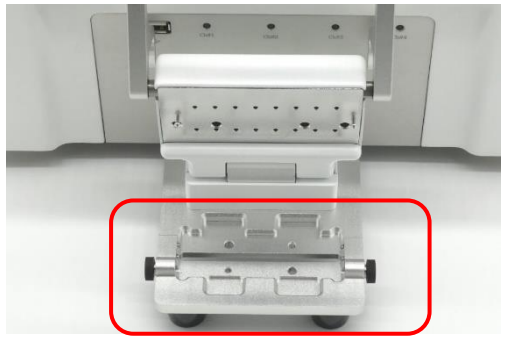
Flex-S workflow

Step 1: Preparation

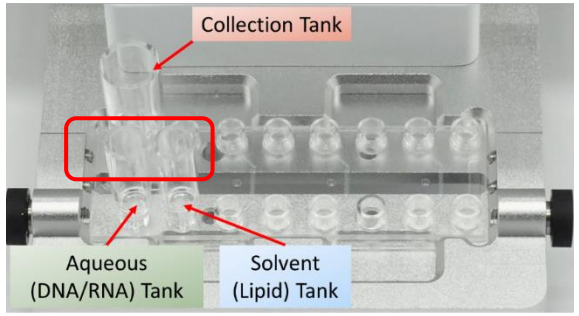


Aqueous: DNA, mRNA in buffer
Solvent: lipid mix in ethanol
(Lipid-Flex formulation)

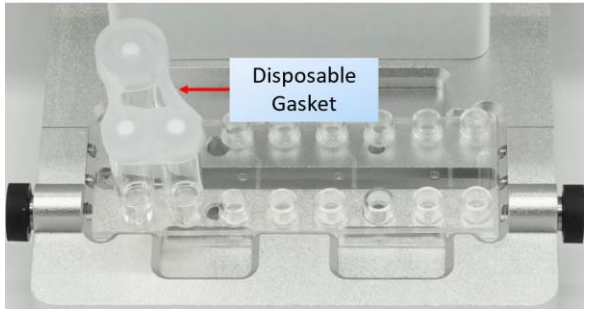
Step 2: Load chip



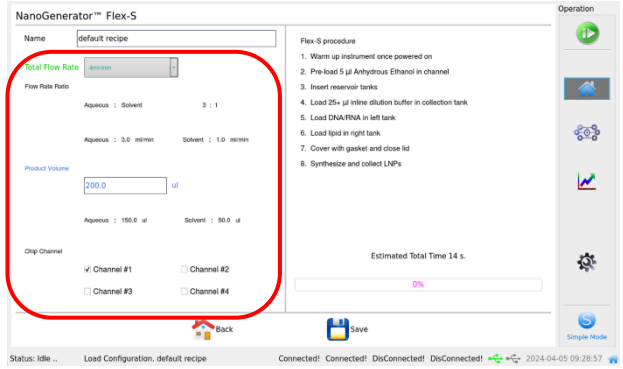
Step 3: Load samples



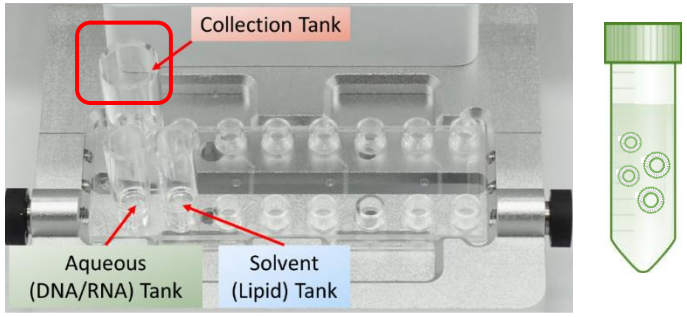
Step4: Put on Gasket



Step 5: Set Parameters and Run



Step 6: Collect LNPs in seconds

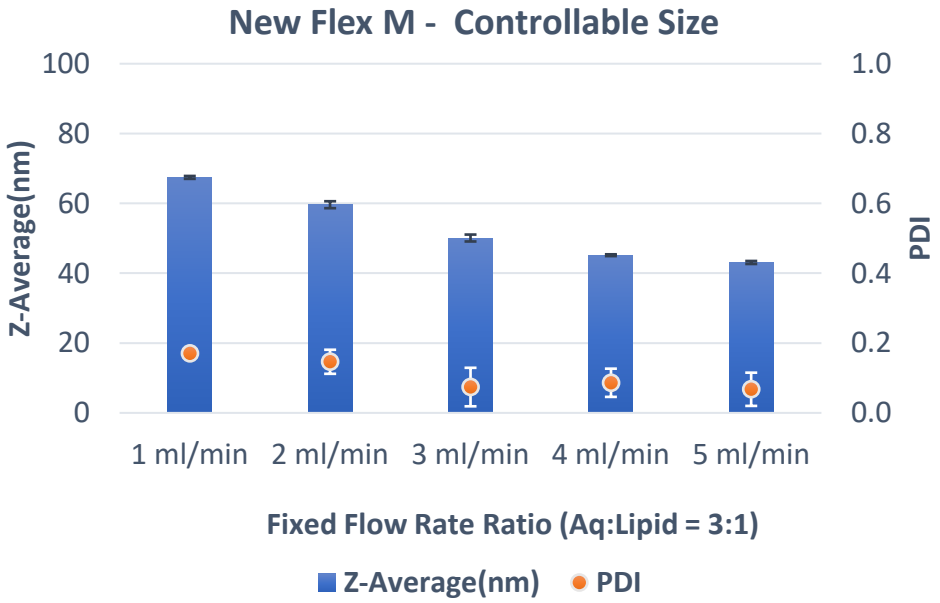


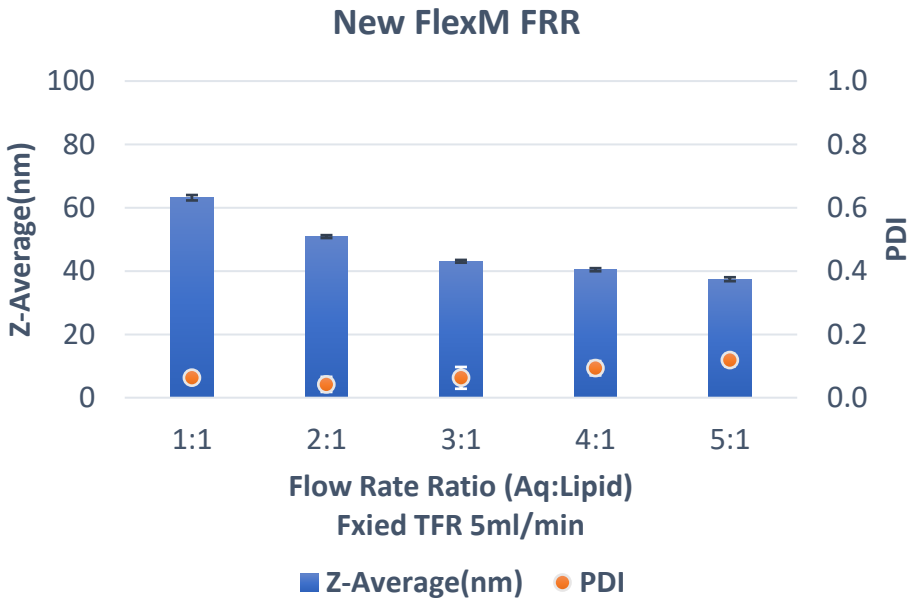
Demo video: [PreciGenome Lipid Nanoparticle Synthesis System NanoGenerator (3gen) Flex-S Demo and Introduction (youtube.com)]
Demo video (muti-channel synthesis): [4 Samples per run for Lipid Nanoparticle Synthesis, NanoGenerator (3gen) Flex-S Demo (youtube.com)]

NanoGenerator® Flex-M

- 1 – 12mL synthesis volume per batch
- Tunable total flow rate (TFR, 1 – 5 ml/min) and flow rate ratio (FRR, 2:1 to 5:1) in Flex-M

NanoGenerator®
Flex-M/Flex-M Premium



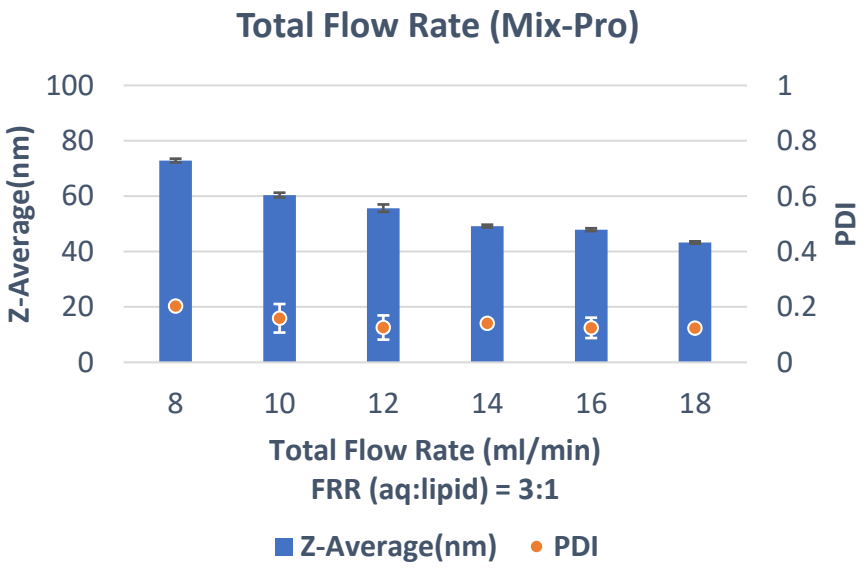


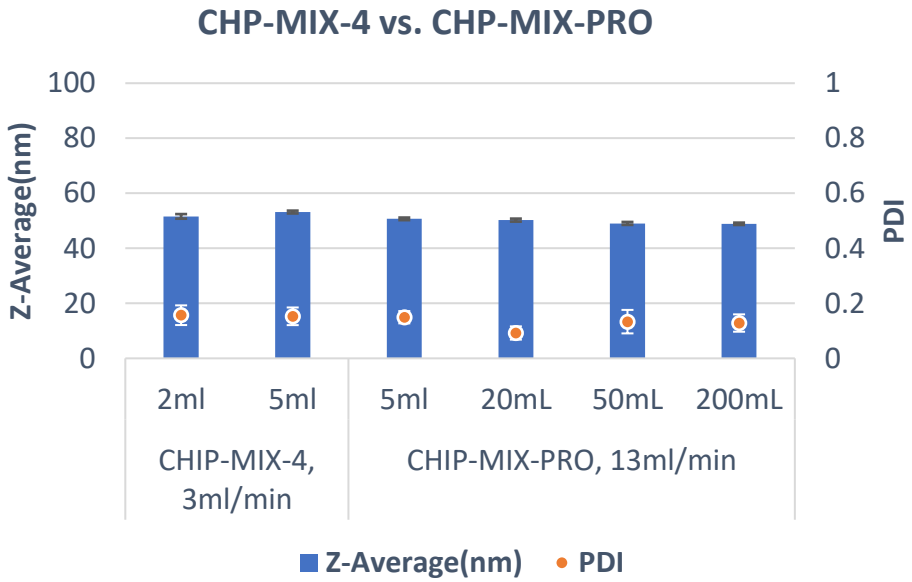
Model	Flex-M
Aqueous phase	Sodium acetate buffer, 100mM, pH5.2
Solvent phase	Lipidflex, 15mM in ethanol

Upgrade Flex-M to Flex-M Premium

- Extend to 75mL synthesis volume per batch
- Tunable total flow rate (TFR, 1 – 5 ml/min) and flow rate ratio (FRR, 2:1 to 5:1) in Flex-M
- Compatible with CHP-MIX-PRO Chip (up to 24 ml/min)

NanoGenerator®
Flex-M/Flex-M Premium





CHP-MIX-PRO

- Total flow rate: up to 24 ml/min
- Through put: 5-75 ml

Model	Flex-M/Flex-M Premium
Aqueous phase	Sodium acetate buffer, 100mM, pH5.2
Solvent phase	Lipidflex, 15mM in ethanol

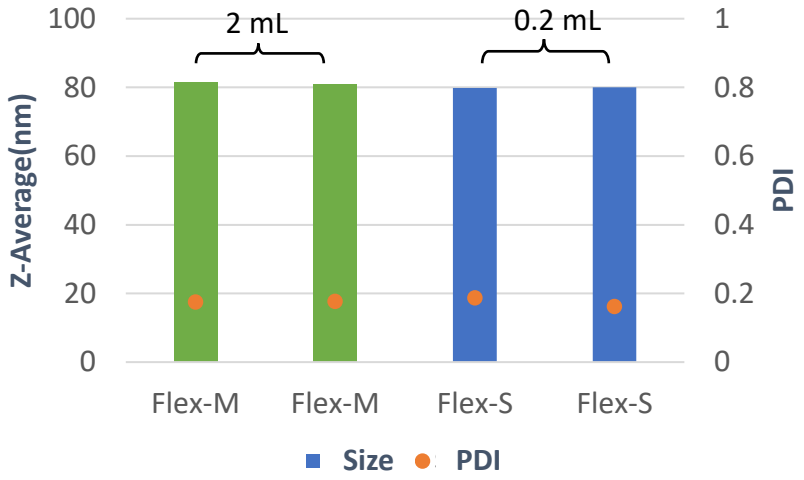
Transferable results between Flex-S/M

- The mixing chip (CHP-MIX-4) is compatible for both Flex-S and Flex-M models.
- Customer can transfer their early screening results to later stage production seamlessly.

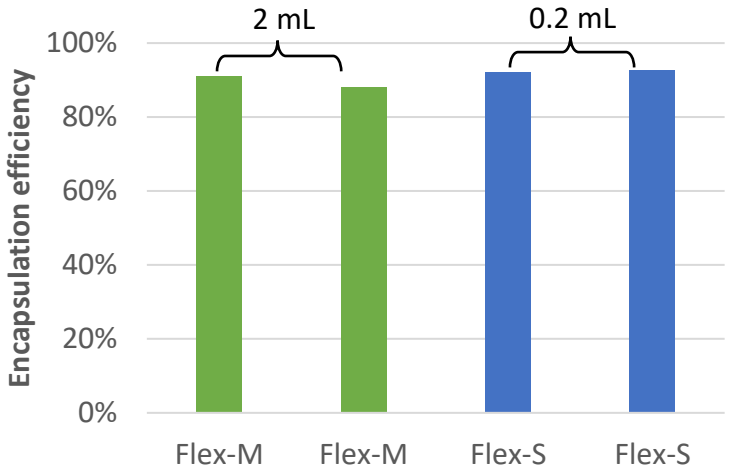
NanoGenerator® Flex-S

NanoGenerator®
Flex-M/Flex-M Premium

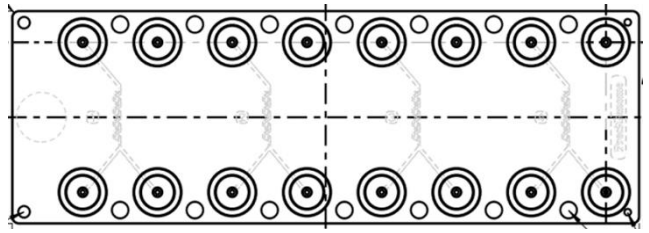
DNA LNP Synthesis



High Encapsulation Efficiency



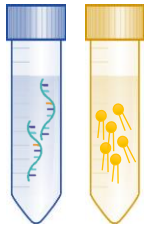
Model	Flex-S/M
Aqueous phase	GFP DNA plasmid (100ug/mL) in sodium acetate buffer(100mM, pH5.2)
Solvent phase	SM102/Lipidflex (40/60 mol%, 12.5mM total lipid concentration) in ethanol
N/P ratio	6



CHP-MIX-4

Flex-M/Flex-M Premium workflow

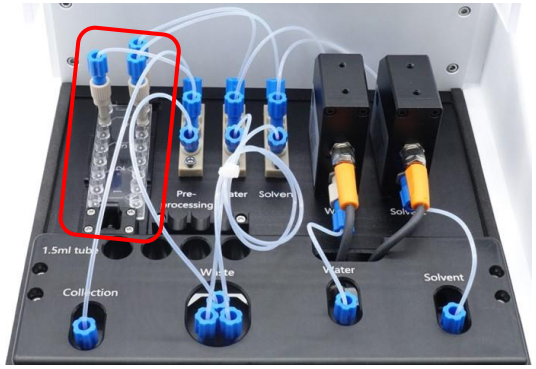
Step 1: Preparation



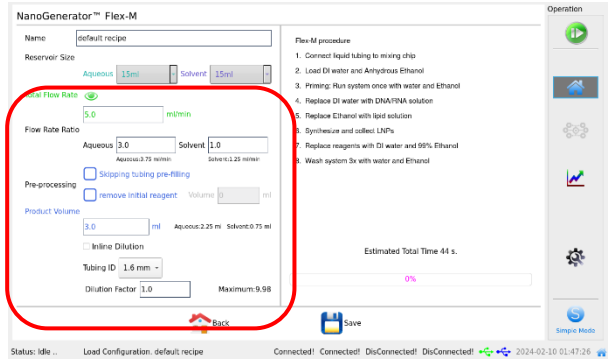
Aqueous: DNA, mRNA in buffer
Solvent: lipid mix in ethanol
(Lipid-Flex formulation)

Step 2: Load sample tubes and collection tube

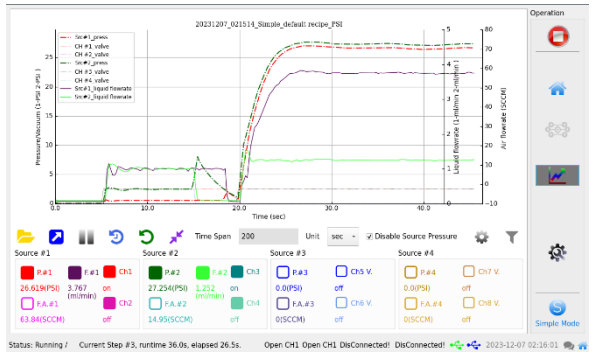
Step 3: Load chip



Step 4: Set parameters and Run



Step 5: Monitor flow rates



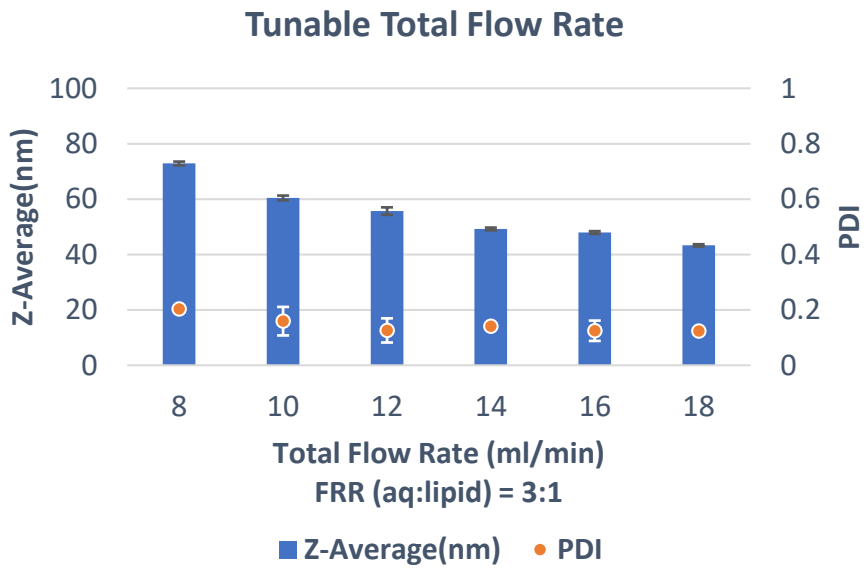
Step 6: Collect LNPs in seconds

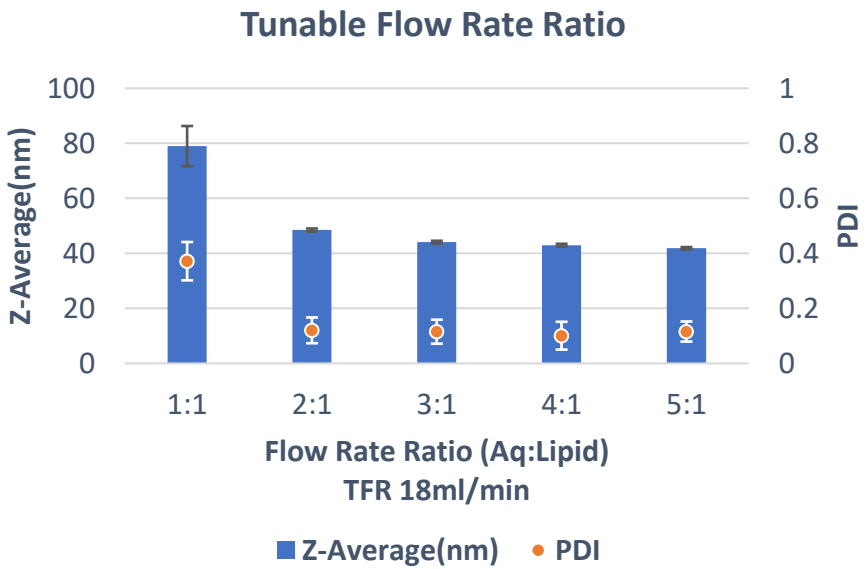
Demo video: [NanoGenerator Flex-M(3Gen) Demo for Lipid Nanoparticles LNP, liposome synthesis (youtube.com)]

NanoGenerator® Pro

- More powerful pump, higher total flow rate.
- Mixing Chip: CHP-MIX-4, CHP-MIX-PRO
- Throughput: 2 – 200 mL
- Total flow rate: up to 24 ml/min
- Flow rate ratio (W:O): 2:1 to 5:1

NanoGenerator® Pro

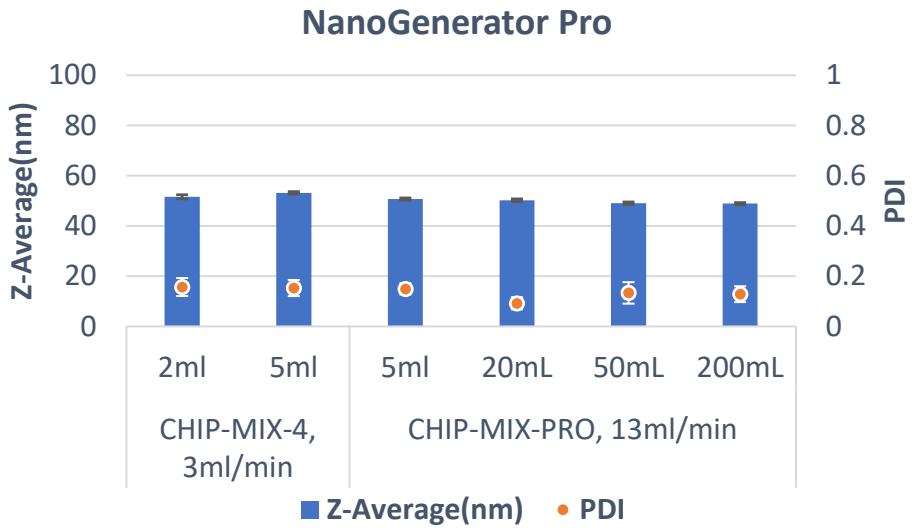




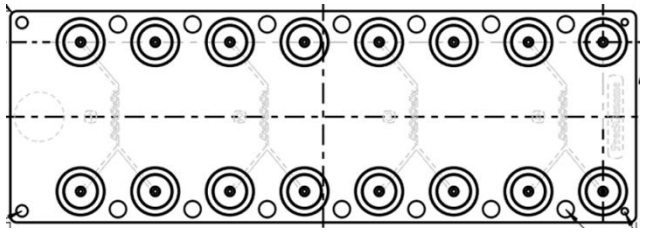
Model	Pro
Aqueous phase	PBS
Solvent phase	LipidDemo, 15mM in ethanol

NanoGenerator Pro

- Mixing Chip: CHP-MIX-4, CHP-MIX-PRO
- Throughput: 2 – 200 mL
- Total flow rate: up to 24 ml/min
- Flow rate ratio (W:O): 2:1 to 5:1



NanoGenerator® Pro



CHP-MIX-4

- Total flow rate: 1 – 5 ml/min
- Throughput: 2 – 12 ml

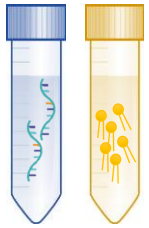
CHP-MIX-Pro

- Total flow rate: up to 24 ml/min
- Throughput: 5 – 200 ml

Model	Flex M
Aqueous phase	PBS
Solvent phase	LipidDemo, 15mM in ethanol

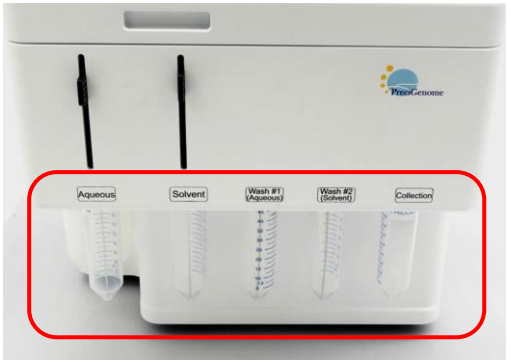
Pro workflow

Step 1: Preparation

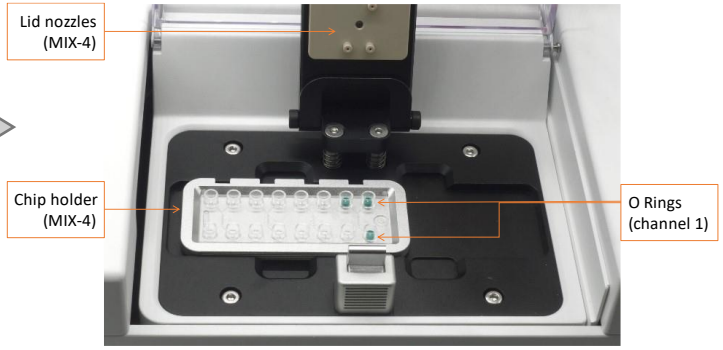


Aqueous: DNA, mRNA in buffer
Solvent: lipid mix in ethanol
(Lipid-Flex formulation)

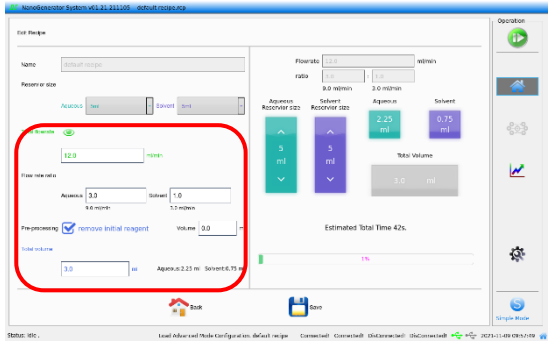
Step 2: Load sample tubes and collection tube



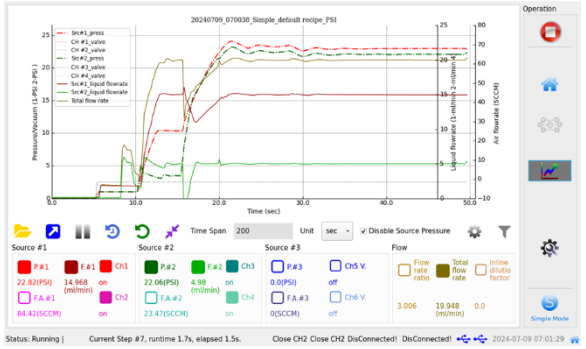
Step 3: Load chip



Step 4: Set parameters and Run



Step 5: Monitor flow rates



Step 6: Collect LNPs in seconds

Demo video: [NanoGenerator Pro Demo for Lipid Nanoparticles LNP, liposome synthesis (youtube.com)]

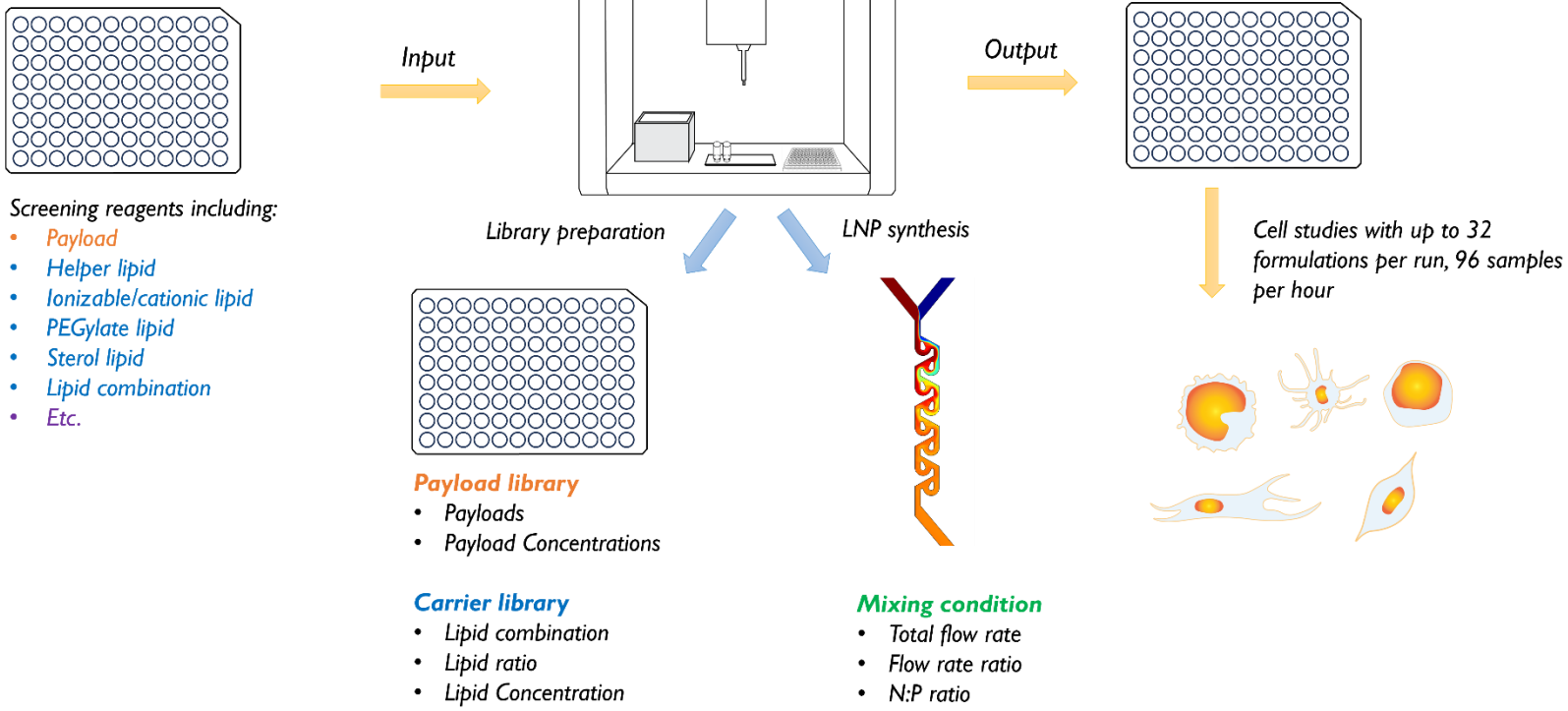
NanoGenerator® Flex-S Plus for screening

NanoGenerator®
Flex-S Plus

- Rapid screening of LNP formulations
- Rapid screening of mRNA/siRNA
- 32 samples per run
- 96 samples within one hour
- Disposable consumables

Model	Flex-S	Flex-S Plus
Multi-sample per run	1 – 4	(1 – 8) × 4 per run Up to 96 samples per hour
Full 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, 4 ml/min
Flow rate ratio	3:1, 4:1	3:1, 4:1
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 molecules, etc.	DNA, mRNA, siRNA, Protein, small molecules, etc.
Dimension	320 mm × 400 mm × 210 mm	630 mm × 570 mm × 660 mm
Weight	8.1 kg	50 kg

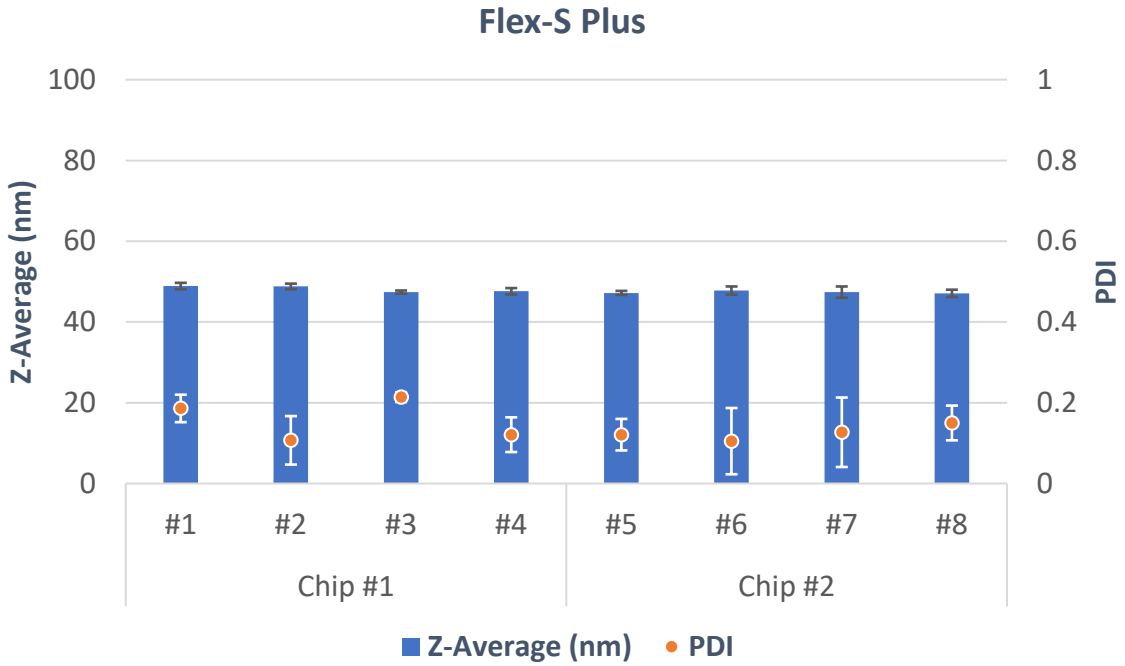
NanoGenerator® Flex-S Plus for screening



Sample Workflow:

1. Load samples in 96 well plates;
2. Seal the 96 well plate (optional);
3. Put consumables on the deck: Chips, 96 well plates, pipette tips, and Gaskets;
4. Set parameters in the software and run the program;
5. Collect samples in 96 well plate;
6. Discard/Change consumable.

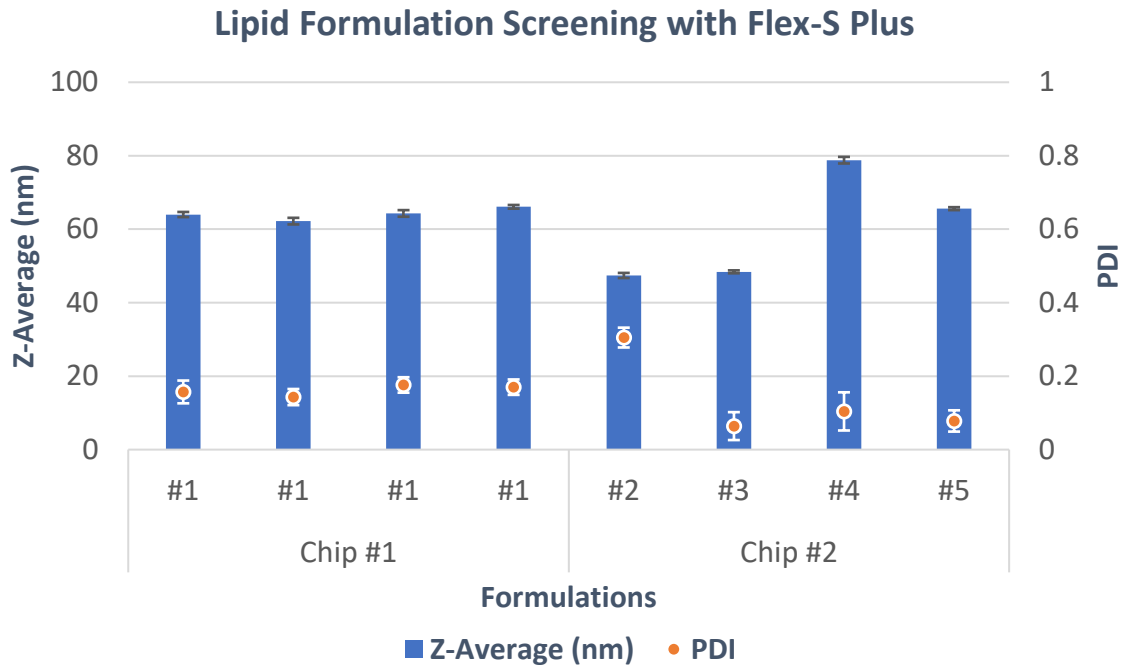
NanoGenerator® Flex-S Plus for screening



- Robust multi-sample synthesis
- Reliable performance
- Consistent results

Model	Flex-S Plus
Aqueous phase	Sodium acetate buffer, 100mM, pH5.2
Solvent phase	Lipidflex, 15mM in ethanol
Parameters	3.3ml/min, FRR 3:1, 200µL

NanoGenerator® Flex-S Plus for screening



- Lipid formulation screening
- 96 samples < 1hour
- 96-well Plate format

Model	Flex-S Plus
Aqueous phase	RNA in Sodium acetate buffer, 100mM, pH5.2
Solvent phase	Different lipid formulation

NanoGenerator® Flex-S Plus

Size (nm)

54.9	45.4	45.5	55.5
54.4	47.6	45	46.2
54.7	46.5	47.4	62.3
54.4	48.2	51.9	57.3
42.6	47.8	44.8	51.2
41.1	50	46.9	48.2
62.8	48.5	46.7	74
56.6	50.7	52.1	59.2

40 80

PDI

0.216	0.13	0.126	0.473
0.175	0.107	0.092	0.08
0.185	0.09	0.104	0.113
0.16	0.1	0.137	0.107
0.306	0.121	0.101	0.403
0.063	0.129	0.128	0.124
0.118	0.066	0.148	0.109
0.041	0.099	0.163	0.113

0.02 0.50

- 32 sample screening (formulation & N:P ratio screening)
- 96 samples < 1hour
- 96-well Plate format

Model	Flex-S Plus
Aqueous phase	RNA in Sodium acetate buffer, 100mM, pH5.2
Solvent phase	Different lipid formulation

Case Study: mRNA LNP for T cell Transfection

eGFP mRNA Lipid Nanoparticles by Flex-S

Z-Average Diameter: 67.3 nm

PDI: 0.106

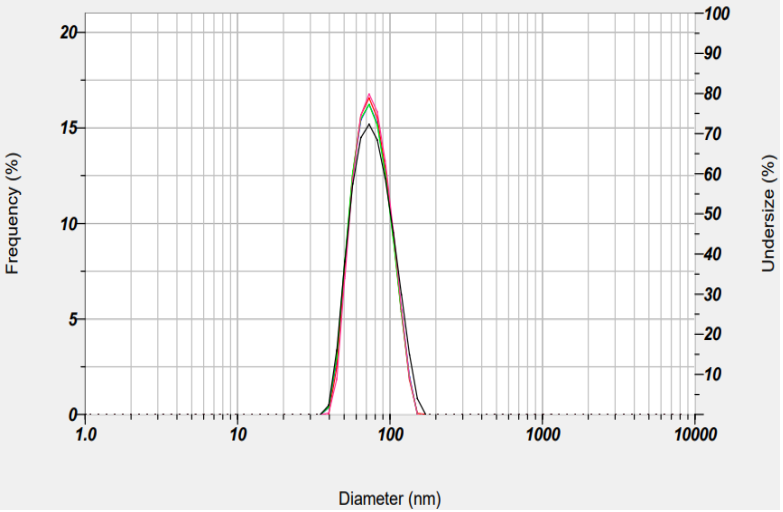


Figure 1. mRNA(eGFP)-LNP Synthesized by NanoGenerator® Flex-S. Average diameter is 67.3 nm. PDI is 0.106. Encapsulation efficiency is 94.5% (Ribo Green RNA Quantification Kit).

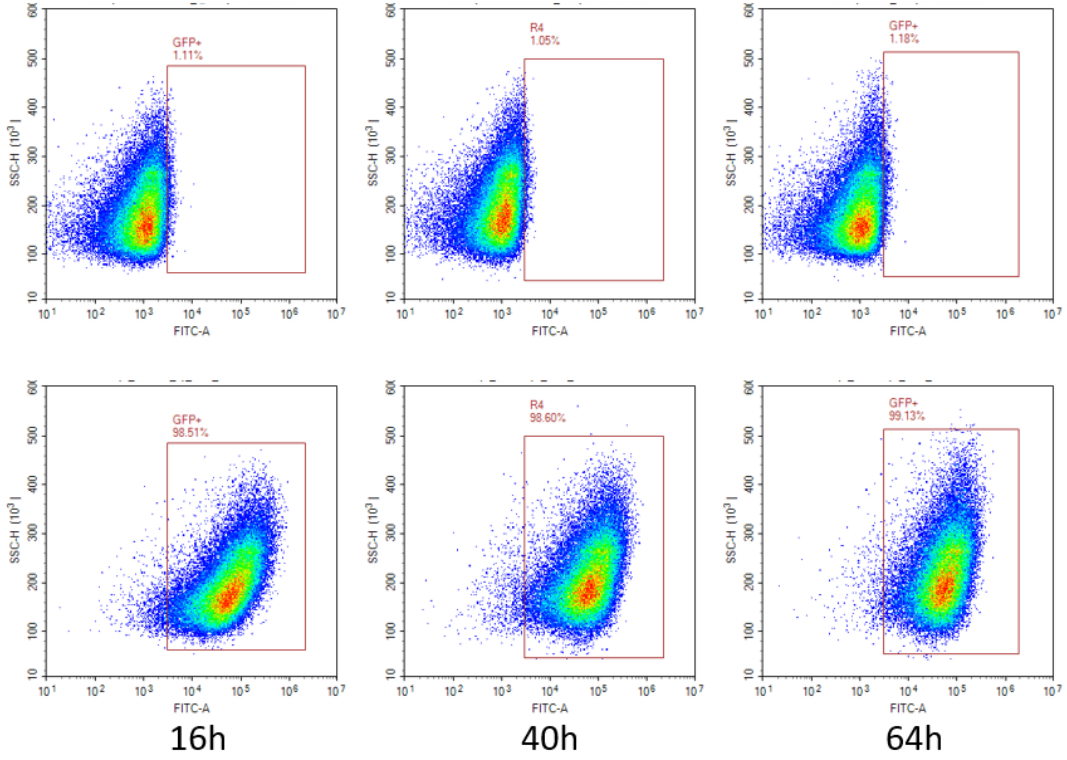
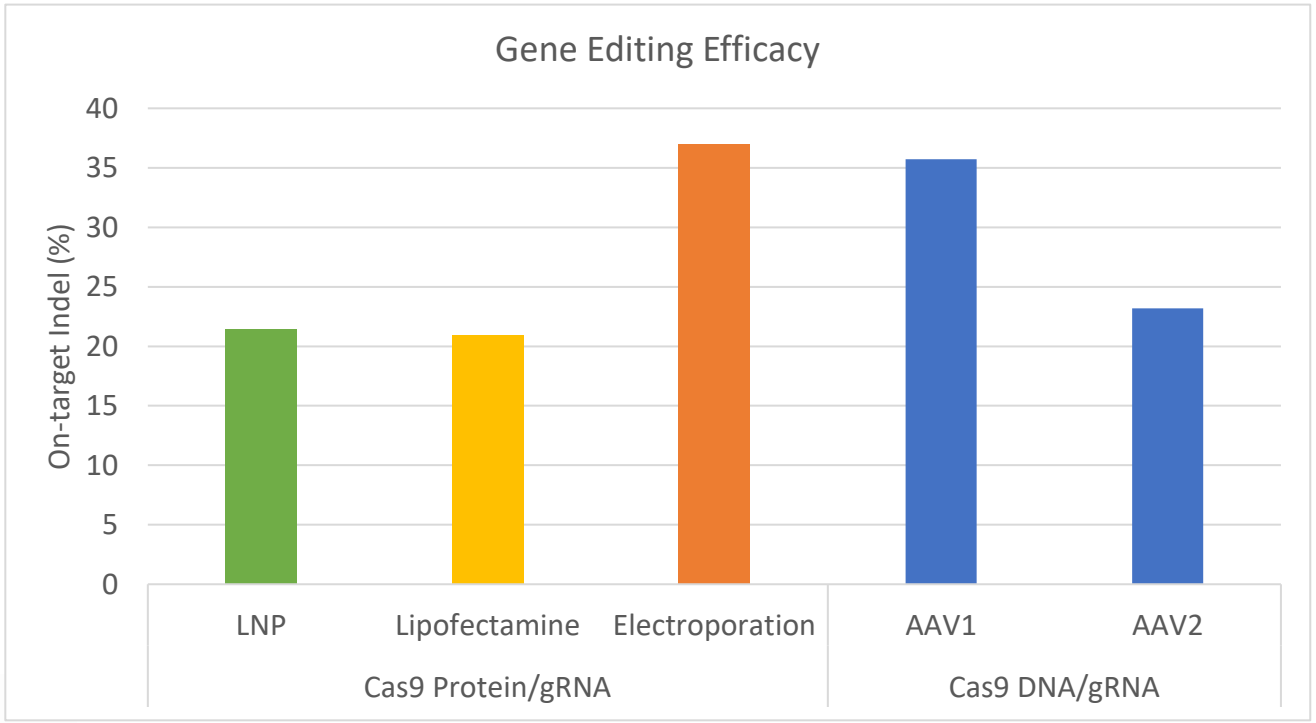


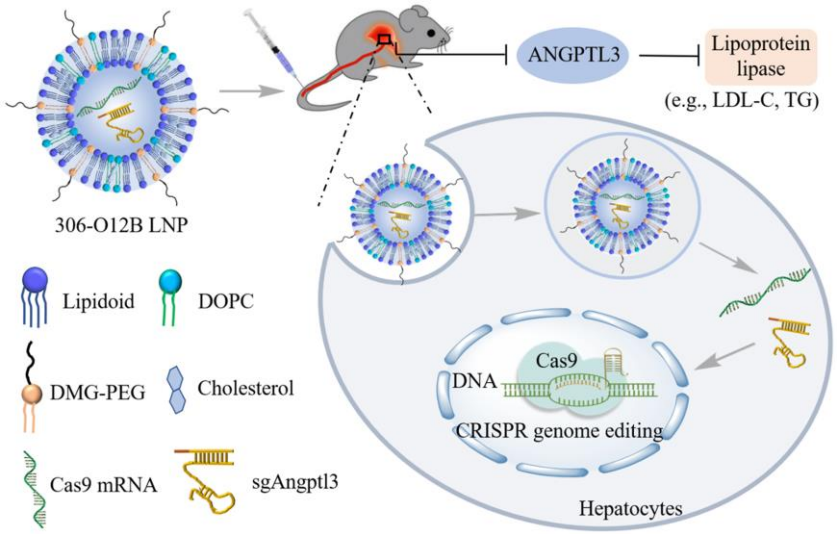
Figure 2. GFP(+) positive population of control (non-treat) and EGFP mRNA LNP treated primary T cells at 16, 40 and 64 hours. Cells were stained (1:50) using Biolegend 7-AAD Viability Staining for 10 minutes. Gating: First select for individual cells (excluding doublets). Then select for the healthy cell population. Then select for viable cells by excluding cells which are positive for 7-AAD. Gate for FitC-A channel (GFP)

Case Study: LNP for Gene Editing

For *in-vitro* gene editing demonstration, Cas9 protein and guide RNA complex was encapsulated in lipid nanoparticle using NanoGenerator Flex-S. The size of resulted LNP was 135nm with a PDI 0.19.

HepG2 cells were treated using Cas9protein/gRNA LNP. Then the gene editing efficacy was determinded throught NGS.





PNAS 2021 Vol. 118 No. 10 e2020401118

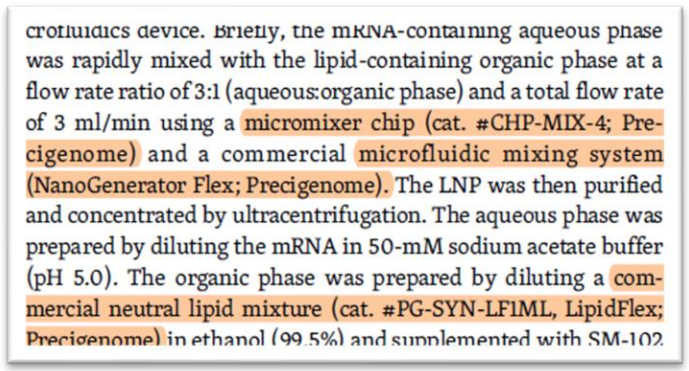
Recent Publications

JEM Journal of Experimental Medicine

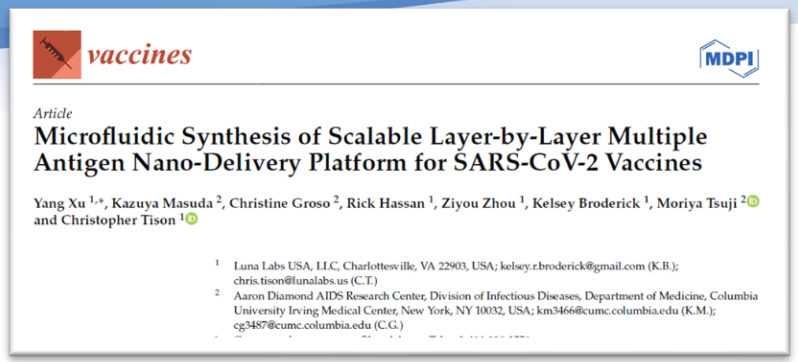
BRIEF DEFINITIVE REPORT

Regenerating murine CD8⁺ lung tissue resident memory T cells after targeted radiation exposure

Mariah Hassert[1], Lecia L. Pewe[1], Rui He[2], Mohammad Heidarian[1,3], Pornpoj Phruttiwanichakun[2], Stephanie van de Wall[1], Madison R. Mix[1,4,5], Aliasger K. Salem[2,4], Vladimir P. Badovinac[1,3,4*], and John T. Harty[1,3,4*]



microfluidics device. Briefly, the mRNA-containing aqueous phase was rapidly mixed with the lipid-containing organic phase at a flow rate ratio of 3:1 (aqueous:organic phase) and a total flow rate of 3 ml/min using a micromixer chip (cat. #CHP-MIX-4; Precigenome) and a commercial microfluidic mixing system (NanoGenerator Flex; Precigenome). The LNP was then purified and concentrated by ultracentrifugation. The aqueous phase was prepared by diluting the mRNA in 50-mM sodium acetate buffer (pH 5.0). The organic phase was prepared by diluting a commercial neutral lipid mixture (cat. #PG-SYN-LF1ML, LipidFlex; Precigenome) in ethanol (99.5%) and supplemented with SM-102



vaccines

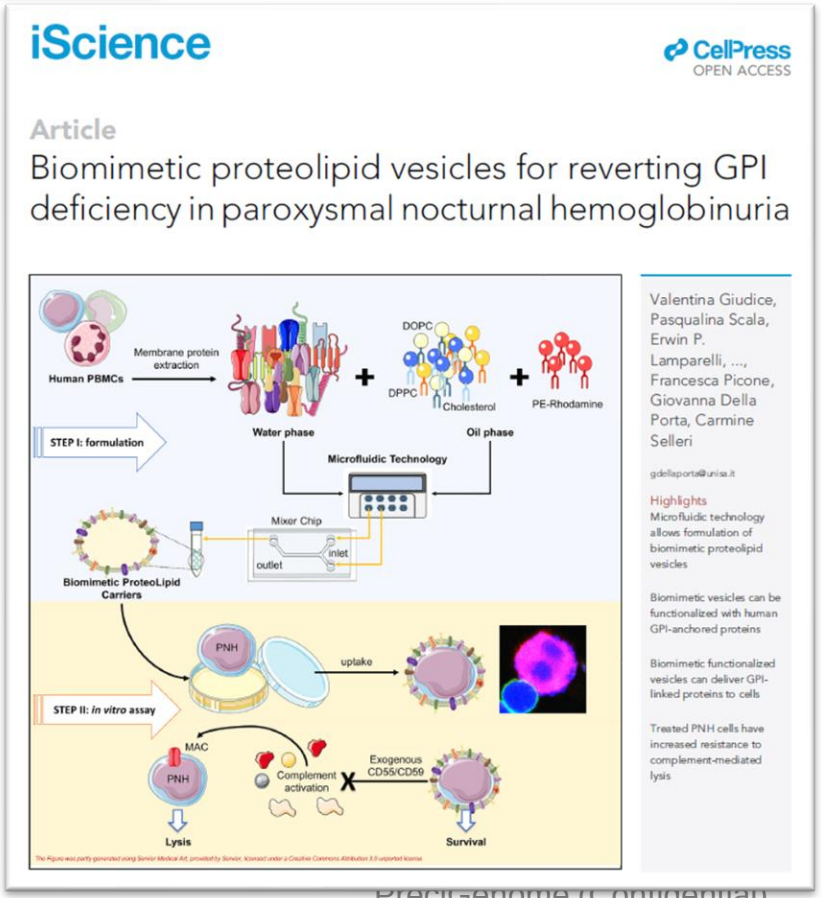
MDPI

Article

Microfluidic Synthesis of Scalable Layer-by-Layer Multiple Antigen Nano-Delivery Platform for SARS-CoV-2 Vaccines

Yang Xu [1,*], Kazuya Masuda [2], Christine Groso [2], Rick Hassan [1], Ziyou Zhou [1], Kelsey Broderick [1], Moriya Tsuji [2] and Christopher Tison [1]

[1] Luna Labs USA, LLC, Charlottesville, VA 22903, USA; kelsey.r.broderick@gmail.com (K.B.); chris.tison@lunalabs.us (C.T.)
[2] Aaron Diamond AIDS Research Center, Division of Infectious Diseases, Department of Medicine, Columbia University Irving Medical Center, New York, NY 10032, USA; km3466@cumc.columbia.edu (K.M.); cg3487@cumc.columbia.edu (C.G.)



iScience

CellPress OPEN ACCESS

Article

Biomimetic proteolipid vesicles for reverting GPI deficiency in paroxysmal nocturnal hemoglobinuria

Valentina Giudice, Pasqualina Scala, Erwin P. Lamparelli, ..., Francesca Picone, Giovanna Della Porta, Carmine Selleri

gdellaporta@unisa.it

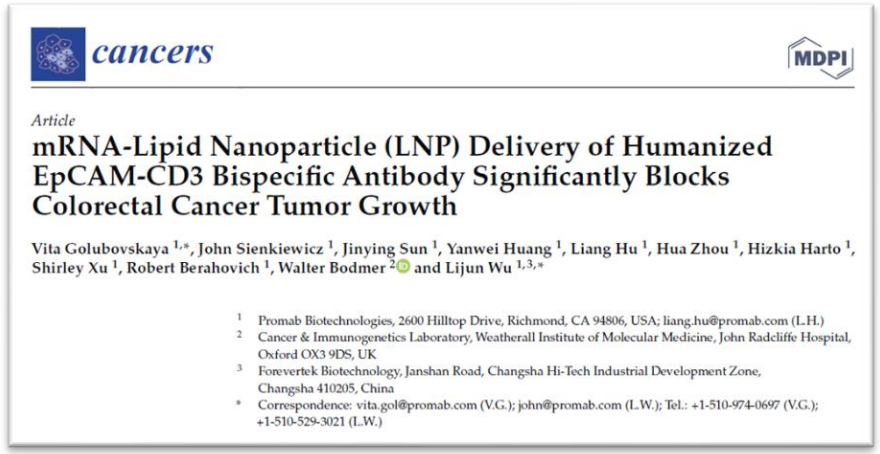
Highlights

Microfluidic technology allows formulation of biomimetic proteolipid vesicles

Biomimetic vesicles can be functionalized with human GPI-anchored proteins

Biomimetic functionalized vesicles can deliver GPI-linked proteins to cells

Treated PNH cells have increased resistance to complement-mediated lysis



cancers

MDPI

Article

mRNA-Lipid Nanoparticle (LNP) Delivery of Humanized EpCAM-CD3 Bispecific Antibody Significantly Blocks Colorectal Cancer Tumor Growth

Vita Golubovskaya [1,*], John Sienkiewicz [1], Jinying Sun [1], Yanwei Huang [1], Liang Hu [1], Hua Zhou [1], Hizkia Harto [1], Shirley Xu [1], Robert Berahovich [1], Walter Bodmer [2] and Lijun Wu [1,3,*]

[1] Promab Biotechnologies, 2600 Hilltop Drive, Richmond, CA 94806, USA; liang.hu@promab.com (L.H.)
[2] Cancer & Immunogenetics Laboratory, Weatherall Institute of Molecular Medicine, John Radcliffe Hospital, Oxford OX3 9DS, UK
[3] Forevertek Biotechnology, Janshan Road, Changsha Hi-Tech Industrial Development Zone, Changsha 410205, China
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Lipid nano-vesicles for thyroid hormone encapsulation: A comparison between different fabrication technologies, drug loading, and an *in vitro* delivery to human tendon stem/progenitor cells in 2D and 3D culture

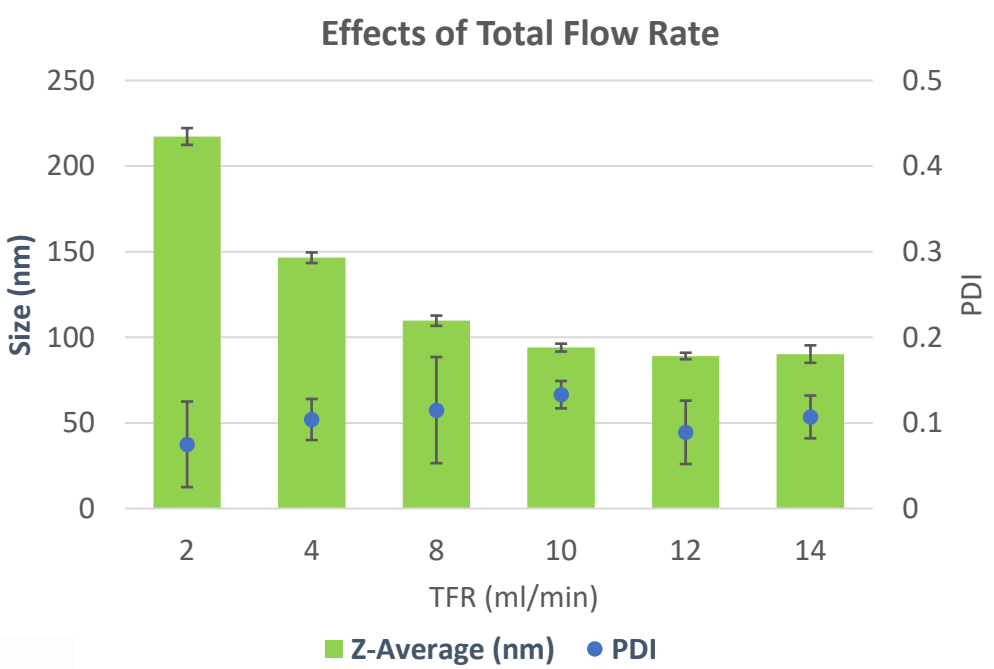
E.P. Lamparelli [a], M.C. Ciardulli [a], P. Scala [a], M. Scognamiglio [b], B. Charlier [a], P. Di Pietro [a], V. Izzo [a], C. Vecchione [a,c], N. Maffulli [a], G. Della Porta [a,b,d,*]

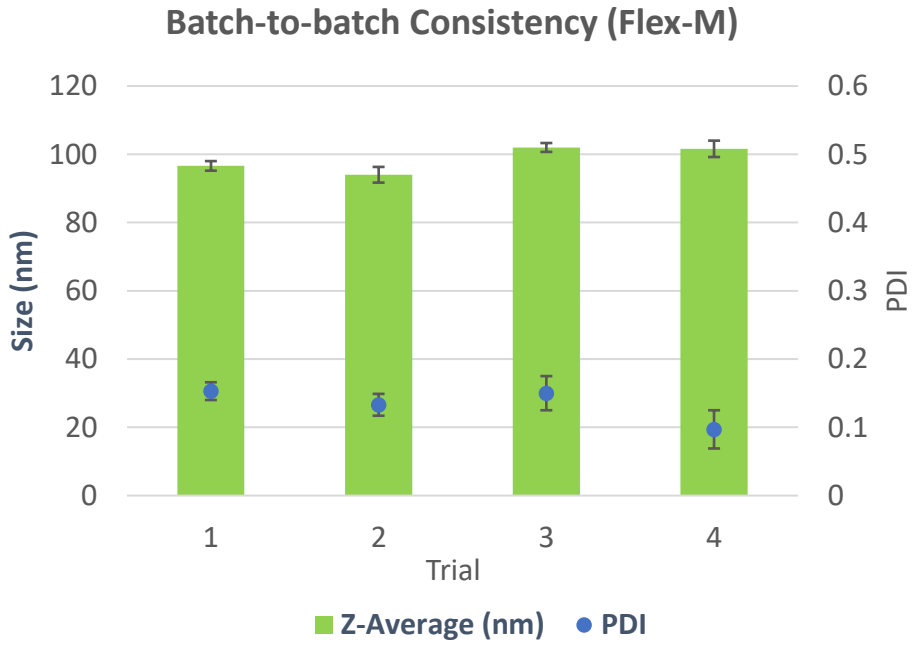
[a] Department of Medicine, Surgery and Dentistry, University of Salerno, Via S. Allende, 84081 Baronissi, (SA), Italy
[b] Department of Industrial Engineering, Università di Salerno, via Giovanni Paolo I, 84084 Fisciano, (SA), Italy
[c] IRCCS Neuromed, Department of Vascular Physiopathology, 86077 Pozzilli, IS, Italy
[d] Interdepartment Centre BIONAM, Università di Salerno, via Giovanni Paolo I, 84084 Fisciano, (SA), Italy

Case Study: PLGA Nanoparticle Synthesis

- PreciGenome's NanoGenerator® is used for the synthesis of a variety of nanoparticles, including PLGA (poly(lactic-co-glycolic acid)) nanoparticles.

- PLGA NP size tuning is controlled by the formulation parameters, the total flow rate and the flow rate ratio.





LipidFlex™ – Flexible Starting Kit

LipidFlex™

Flexible Lipid Nanoparticle Formulation

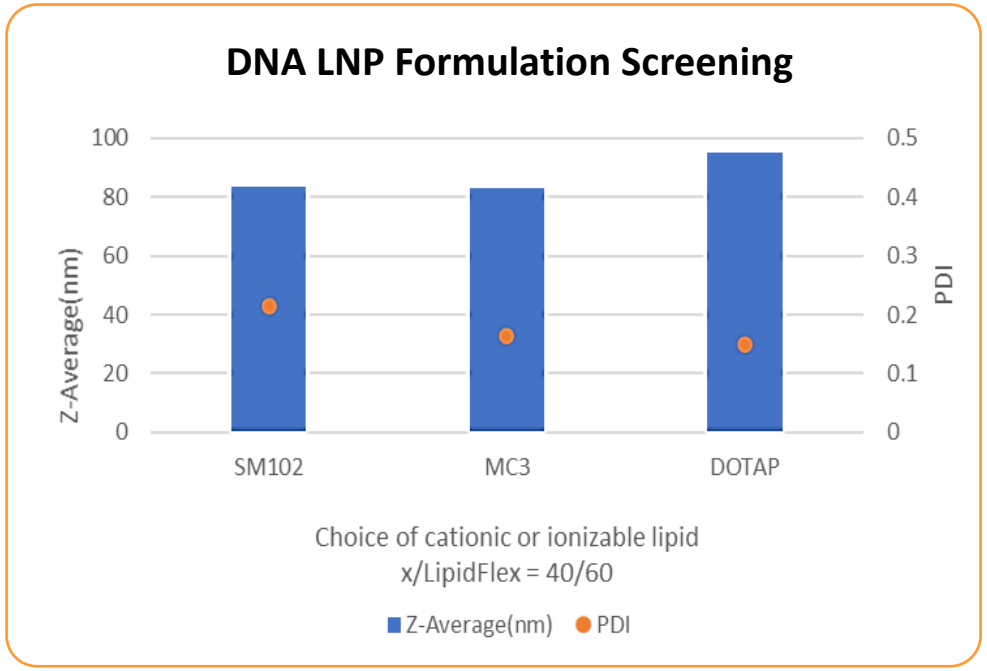
LipidFlex™ is a 3-component lipid nanoparticle formulation that compatible with various cationic/ ionizable lipids for nucleic acid encapsulation and cell transfection. LipidFlex™ Pack kit includes ionizable lipid (SM102).

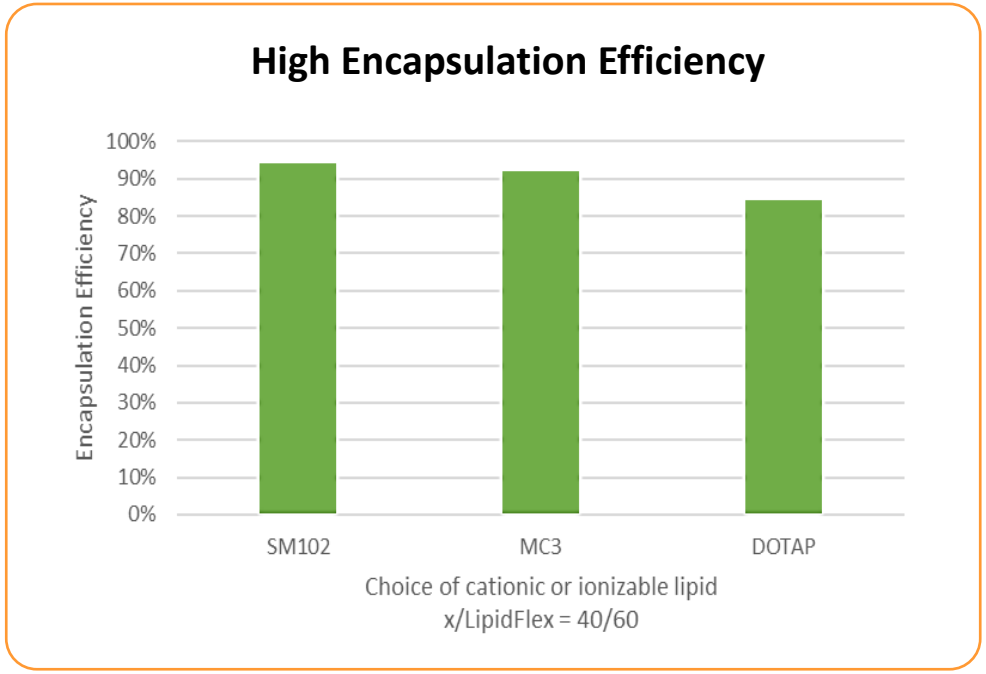
- Flexible cationic/ionizable lipid ratio
- Flexible with various N/P ratio
- High nucleic acid encapsulation efficiency
- High mammalian cell transfection rate

Model	LipidFlex™
Catalog #	PG-SYN-LF1ML
Components	Structural Lipid/ Cholesterol/Stabilizer
Product size	1000 µL
LipidFlex Conc.	30 mM
Ionizable lipid	NA

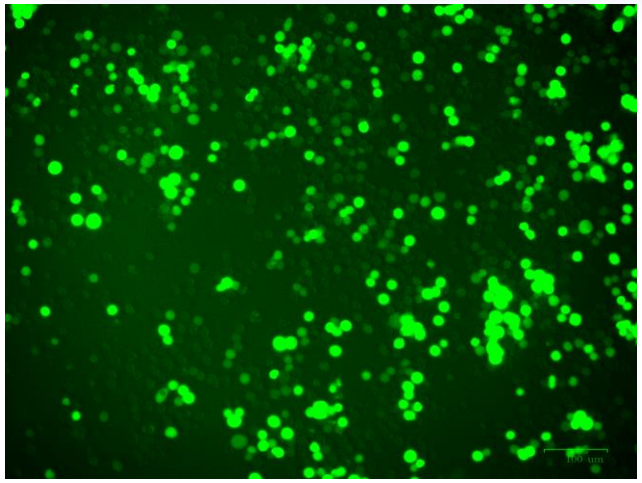
LipidFlex™ – Flexible Starting Kit

- PreciGenome provides a general LipidFlex™ formulation for quick formulation screening.
- By adding cationic/ionizable lipid into LipidFlex™, customer can prepare nucleic acid LNP with high encapsulation efficiency.

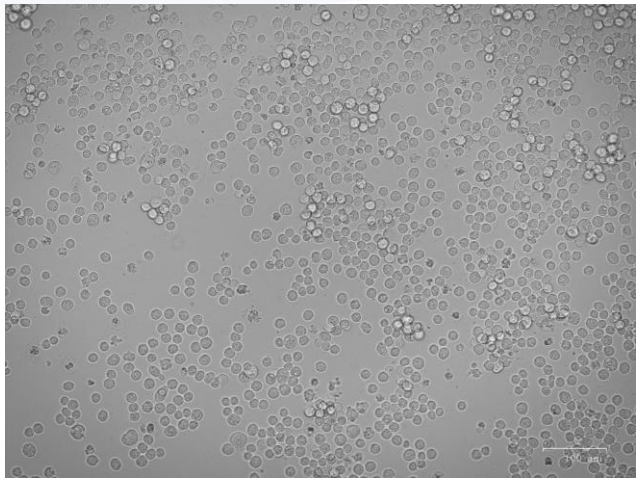




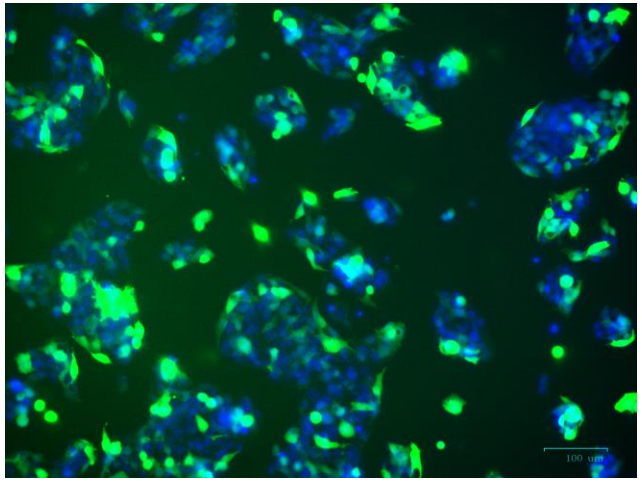
LipidFlex™ LNP – Cell Transfection to Different Cell Lines



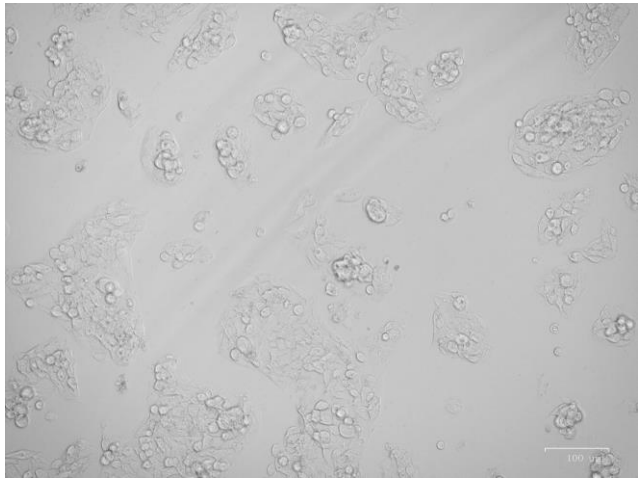
K562 – Green Fluorescence Field



K562 –Bright Field



HepG2 – Green and Blue field overlay

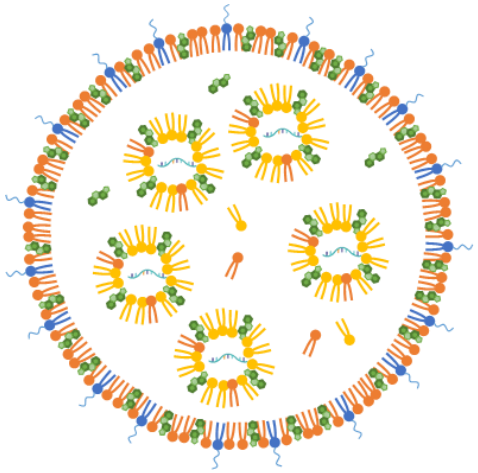


HepG2 –Bright Field

- DNA lipid nanoparticle (gWiz GFP plasmid, Aldervon) was generated using SM102/PG-LipidFlex (40/60 mol%) formulation by PreciGenome NanoGenerator.
- HepG2 and K562 Cell lines are successfully transfected by GFP DNA LNP. 48 hours post transfection, HepG2 Cell nucleuses are stained with Hoechst 33342 dye (blue color) before imaging.

LipidFlex™ T Cell Kit

LipidFlex™ T cell kit is a highly efficient lipid formulation to synthesize mRNA lipid nanoparticles (LNP) for primary human T cell gene delivery. Using NanoGenerator® Flex-S system and CHP-MIX-4 cartridge, customers can prepare potent mRNA LNP in a convenient and efficient way.

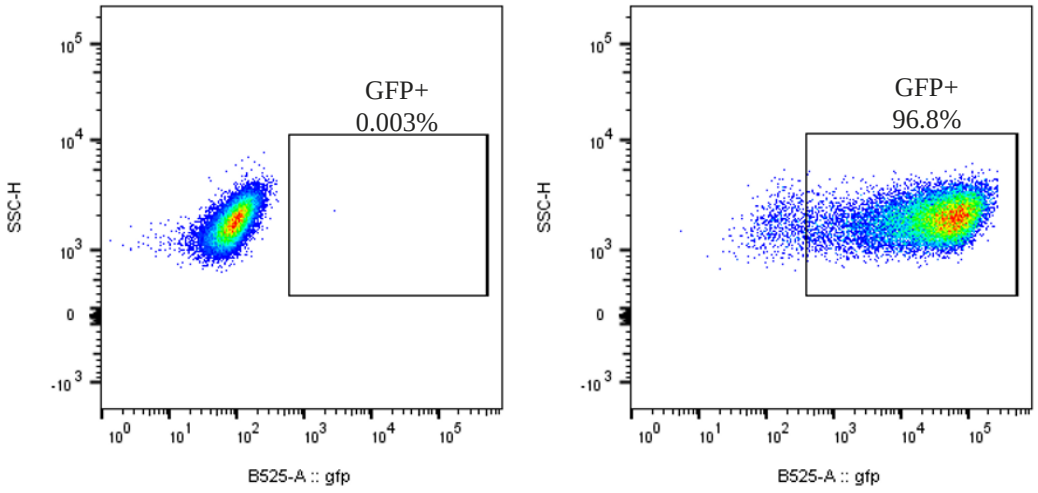


- Over 90% mRNA encapsulation efficiency
- High transfection efficiency
- High protein expression level
- High cell viability
- Time efficient synthesis process

Component	Size	Storage
LipidFlex T cell Lipid mix	125 µL	-80 ˚C
Formulation Buffer 1 (10x)	60 µL	4 - 8 ˚C
Formulation Buffer 2	600 µL	4 - 8 ˚C

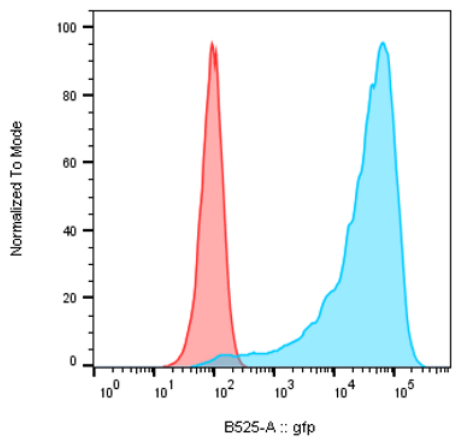
LipidFlex™ T Cell Kit

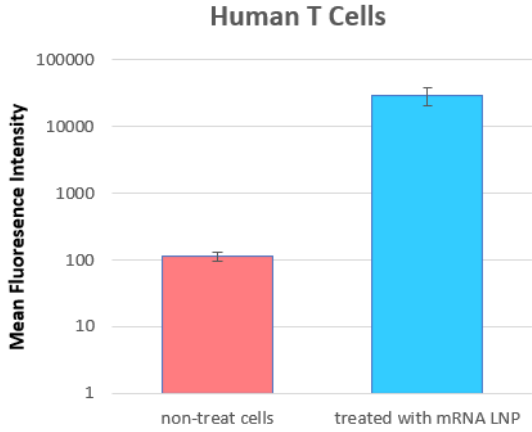
High Human T Cell Transfection Efficiency



* 24 hours post-treatment Human T cells (eGFP mRNA from Trilink)

High Protein Expression Level



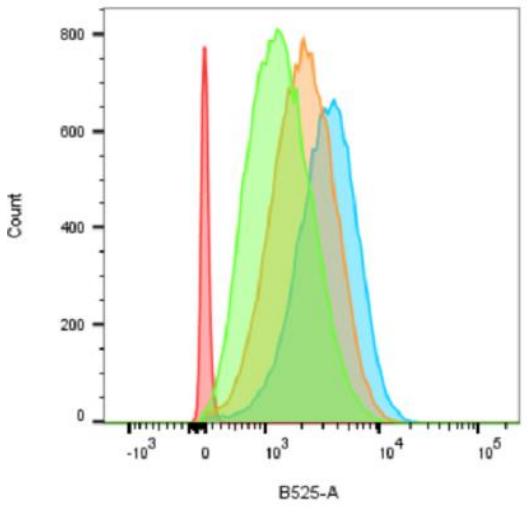


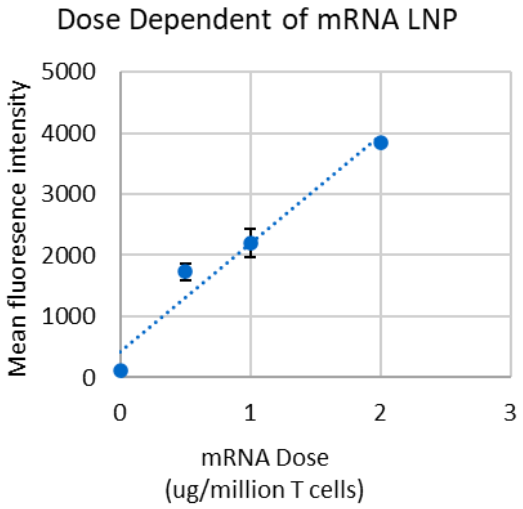
Non-treat cells Treated with eGFP mRNA LNP

* 24 hours post-treatment Human T cells (eGFP mRNA from Trilink)

LipidFlex ™ T Cell Kit

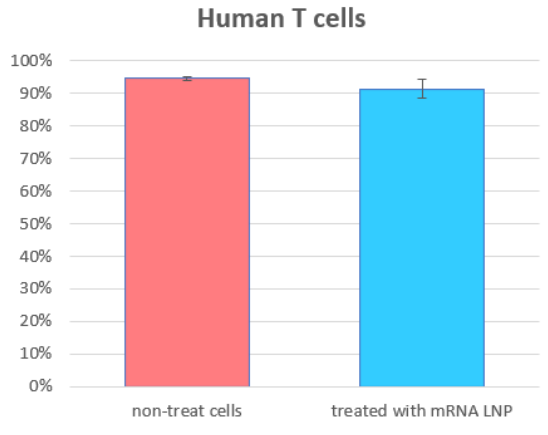
mRNA LNP Dose Dependency

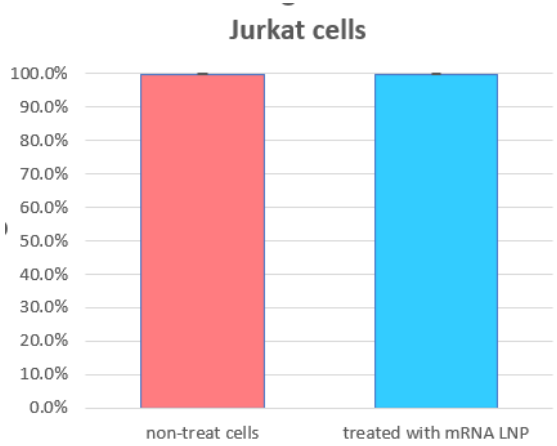




* 24 hours post-treatment Jurkat cells (eGFP mRNA from ProMab)

High Cell Viability





* 24 hours post-treatment Human T cells and Jurkat cells

Why PreciGenome?

NanoGenerator® Flex-M/

High Performance & Efficiency

- Tunable size (40-200nm)
- Low PDI (0.05-0.2)
- High encapsulation efficiency

Open Platform

- Upgradable system
- Transferable microfluidic chips

Scalable Throughput

- Low volume for screening (Flex-S)
- Medium volume production (Flex-M/Flex-M Premium)
- High volume production (Pro, Max-GMP)

NanoGenerator® Flex-M/Flex-M Premium

Simple Operation

- Simple setup
- Compact size
- Intuitive UI w/ touchscreen

Cost Effective

- Affordable configuration
- Lower cost per run

Custom Support

- Demo, Training and Support
- Extended Warranty
- Hot swap option
- Local US company

NanoGenerator® Pro

Some of Our Customers

PreciGenome LLC

Email: contact@precigenome.com

Tel: 1-408-708-4602

Address: 2176 Ringwood Ave.

San Jose, CA, United States 95131

YALE

Cornell University

UNIVERSITY OF WASHINGTON

sorrento THERAPEUTICS

ProMab Biotechnologies, Inc.

KEMIJSKI INŠTITUT

TEXAS The University of Texas at Austin

SPH 上海医药 SHANGHAI PHARMA

Children's Hospital LOS ANGELES

LUNA

WALKING FISH THERAPEUTICS

AURIGENE PHARMACEUTICAL SERVICES

FormuMax

Comparison with Other LNP Synthesizer

Formulation of PolyA RNA-LNP

NanoAssemblr benchtop

NanoGenerator™ Flex-M nanoparticle synthesis syste

N/P: 4:1

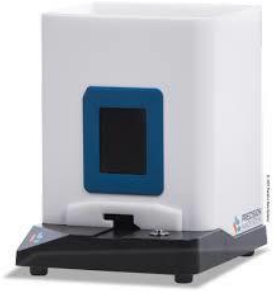
Total Flow Rate: 12 mL/min

	PolyA LNP
Size (nm) in PBS	68.2 ± 0.5
PDI	0.182 ± 0.016
ζ-potential (mV)	-5.31 ± 6.03
EE (%)	97.9

Total Flow Rate: 3 mL/min

	PolyA LNP
Size (nm) in PBS	70.7 ± 1.2
PDI	0.172 ± 0.029
ζ-potential (mV)	-6.20 ± 6.53
EE (%)	95.6

Comparison with Other LNP Synthesizer



	Flex-S	Spark
Sample 1	87 nm	117nm
Sample 2	151 nm	201 nm

- Feedback:
  Spark uses 2ml/min and 2:1, ratio is not changeable. The size is 20-30% larger.

Comparison with Different T-cell kits

Sample	Encapsulation %	Size_before_spin (nm)	PDI	Size_after_spin (nm)	PDI
GFP_PreciLipid_FlexS	91.5	70	0.147	71	0.136
GFP_PniLipid_FlexS	98	87	0.211	NA (defective column)	

Flex-S. PNI_lipid.GFP.NP=6

87nm

Flex-S. Precigenome_lipid.GFP.NP=6

70 nm