Product Catalog

NanoGenerator™
Nanoparticle Synthesis

NanoGenerator™
Nanoparticle Synthesis System

Nanoparticle synthesis by microfluidic technology presents advantages over the conventional batch synthesis processes due to its superior control of size and shape.

PreciGenome's NanoGenerator™ applies microfluidic approaches to synthesize nanoparticles in a continuous mode. The systems have been widely used in various applications in the drug delivery field, such as lipid nanoparticles (LNP), liposomes, PLGA nanoparticles etc.

Microfluidic Mixing System

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

Payloads

- DNA/mRNA/siRNA
- Proteins and peptides
- Small molecule drugs
- Other payloads

System Benefits

High Performance & Efficiency

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

Open Platform

- Reagents
- Microfluidic chips

Scalable Throughput

- Flex S: 0.2-2 mL
- Flex M: 1-12 mL
- Pro/Max: 200mL/1L+

Simple Operation

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

Cost Effective

- Affordable configuration
- Low cost consumables

Custom design &OEM

- Research collaboration
- Custom design
- OEM & Contract manufacturing

Catalog #	Name
PG-SYN-FS	NanoGenerator^{TM} Flex-S
PG-SYN-FM	NanoGenerator^{TM} Flex-M
PG-SYN-F	NanoGenerator^{TM} Flex (S+M)
PG-SYN-P	NanoGenerator^{TM} Pro
PG-SYN-G	NanoGenerator^{TM} Max (GMP)

NanoGenerator™ System Models

Discovery & Screen

NanoGenerator™ Flex

Scientific research, screening and discovery for quick low-volume preparation

Flex-S: 0.2 to 2 mL throughput
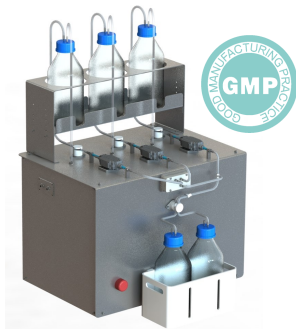Flex-M: 1 to 12 mL throughput

Screen & Develop

NanoGenerator™ Pro

Preclinical Studies and Development

Pro: 2 to 200 ml throughput

Scale-up

NanoGenerator™ Max (cGMP version)

Clinical development
cGMP certified manufacturing

Max: 1L throughput
Max+:   >10 L throughput
(available soon)

Custom solution

NanoGenerator™ OEM

Custom design and OEM solutions
GMP certified manufacturing

High volume: >20 L throughput
High throughput: 32/64 samples per run

System Applications

Nucleic Acid Lipid Nanoparticles	**Liposomes**	**Polymer Nanoparticles**
• mRNA vaccines • Rare genetic diseases • Gene & cell therapy • CAR-T therapeutics	• Cancer therapy • Vaccine Adjuvant • Antimicrobial therapy • Cosmetics	• Cancer chemotherapy • Immunology & vaccines • Insulin delivery for diabetes

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# NanoGenerator™ Flex-S Nanoparticle Synthesis System

NanoGenerator™ Flex-S nanoparticle synthesis system

PreciGenome's NanoGenerator™ Flex-S design is for small scale production. The throughput volume range is from 0.2 to 2 mL, which is perfect for formulation screening and early discovery applications.

Smaller output volume (<0.2ml per run) is achievable by recipe optimization.

Model	NanoGenerator™ Flex-S
Mixing Cartridge	CHP-MIX-4
Throughput	0.2 to 2 mL
Total Flow Rate	3 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
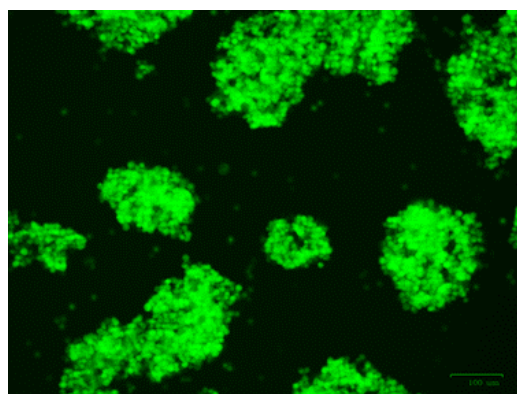
Jurkat Cells transfected with Formulation #9. Green fluorescence image at 48 hours post transfection.

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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# NanoGenerator™ Flex-M Nanoparticle Synthesis System

NanoGenerator™ Flex-M nanoparticle synthesis system

PreciGenome's NanoGenerator™ applies microfluidic approaches to synthesize nanoparticles (LNP, liposome, PLGA, etc.) in a continuous mode. NanoGenerator™ Flex-M system provides a wide throughput range from 1 to 12 mL, which meets a variety of applications from early screening to animal study.

Flex-M system also provides in-line dilution option to reduce ethanol concentration instantly. It further stabilizes LNP products.

Model	NanoGenerator™ Flex-M
Mixing Cartridge	CHP-MIX-4
Throughput	1 to 12 mL
Total Flow Rate	1 to 3 mL/min
Flow Rate Ratio (W:O)	2:1 to 5:1
In-line Dilution (optional)	0.5:1 to 2:1
Size Range	40 to 200 nm
PDI	0.05 to 0.2
Encapsulation Efficiency	85-95%

Tunable Parameter—Flex M
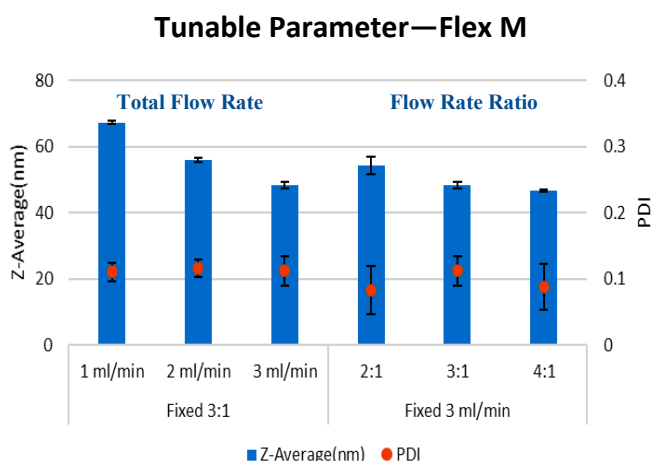
mRNA LNP Synthesis
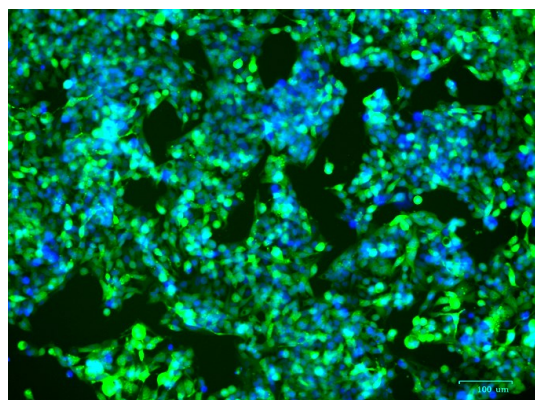
HepG2 cells were successfully transfected by eGFP mRNA LNP. Cell nucleuses were stained with Hoechst 33342 dye (blue color) before imaging.
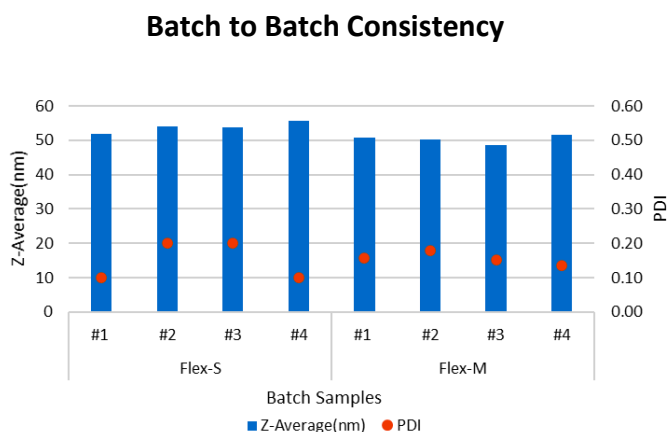
Batch to Batch Consistency

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Case Study:

T Cell Transfection by mRNA Lipid Nanoparticles

Since the first FDA approval of chimeric antigen receptor (CAR) T cell therapy in 2017, T cell engineering is continuously the hottest research field in immunotherapy and cell therapy. Current CAR T cell engineering methods use viral transductions, which induce permanent CAR expression and have potential safety concerns. To overcome this concerns, researchers are highly interested in non-viral gene delivery methods.

Recently, CAR mRNA lipid nanoparticles (LNPs) in T cell engineering have been widely studied. The transient transduction feature of mRNA LNP make it a safer profile than viral vectors. The size, homogeneousness and mRNA encapsulation efficiency are the key factors for efficient T cell transfection. Using PreciGenome's NanoGenerator™ system, customer can produce mRNA LNPs with well controlled size, high homogeneousness and excellent encapsulation efficiency.

The following data shows the size and PDI of GFP mRNA lipid nanoparticles synthesized by NanoGenerator™ Flex system. The transfection efficiency to K562 and HepG2 cell lines and human primary T cells are presented in Figure 2 and 3.
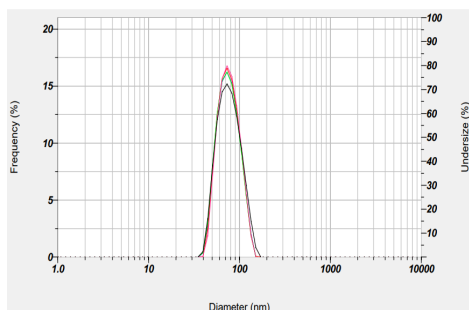

Figure 1. GFP-LNP Synthesized by PreciGenome's NanoGenerator™ Flex-S. Average sizes is 67.3 nm. PDI is 0.106.
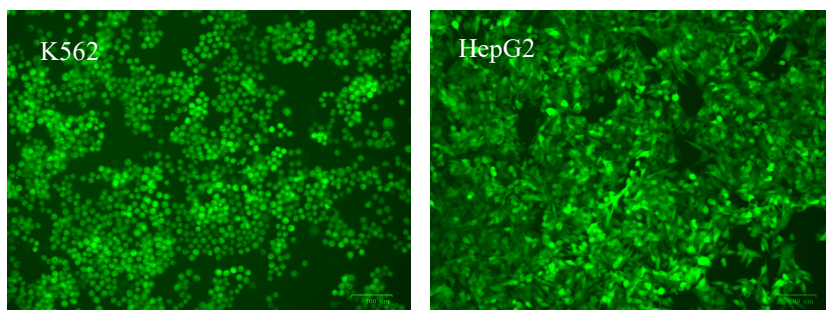

Figure 2. GFP expression in K562 (left) and HepG2 (right) cell lines after 48 hours treated by GFP-LNP synthesized by PreciGenome's NanoGenerator™ Flex-S.

Figure 3. GFP(+) positive population of control (non-treat) and eGFP LNP treated primary T cells at 16, 40 and 64 hours.
Cells were stained (1:50) using Biolgend 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)
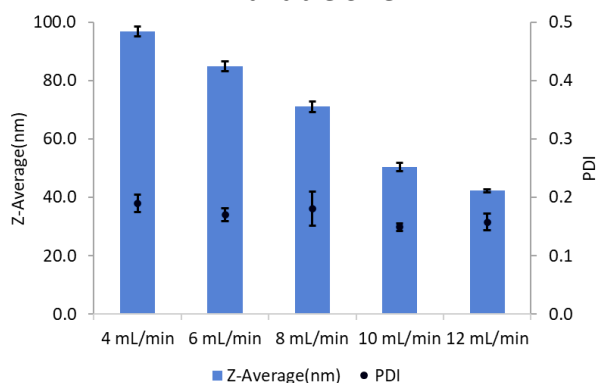
Non-treated T cells

GFP-LNP treated T Cells

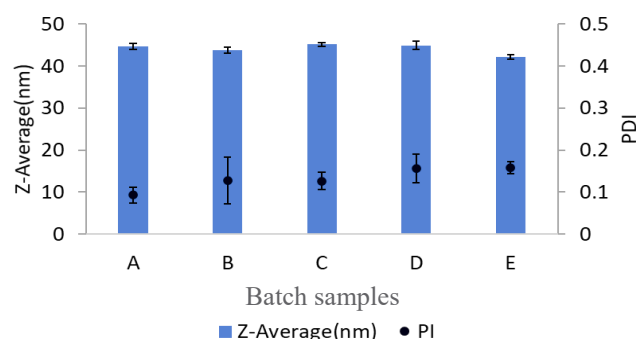16h   40h   64h
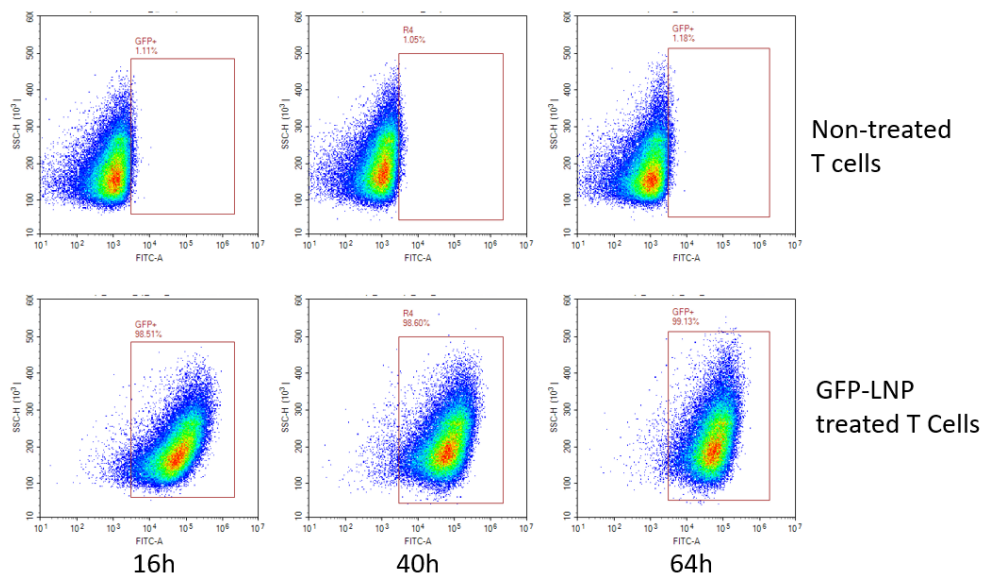
NanoGenerator™ Pro
Nanoparticle Synthesis System

PreciGenome's NanoGenerator™ Pro is an integrated nanoparticle synthesis system. NanoGenerator™ Pro contains more powerful pressure control modules, which provides higher throughput from 2 to 200 mL. The total flow rate range is from 4 to 12 mL/min. The flow rate ratio (W:O) is between 2:1 to 5:1.
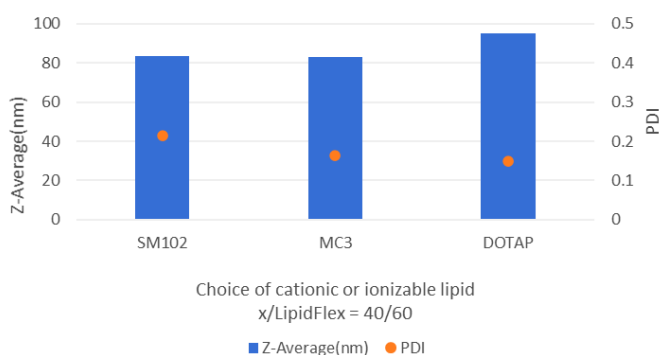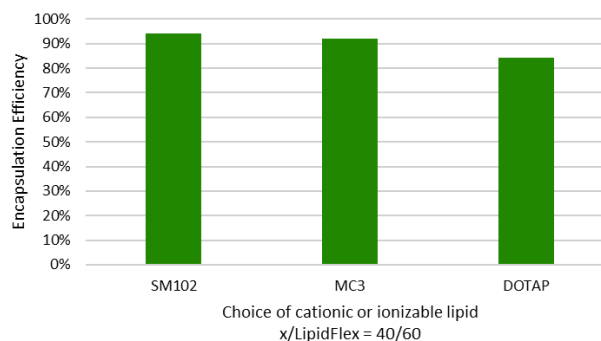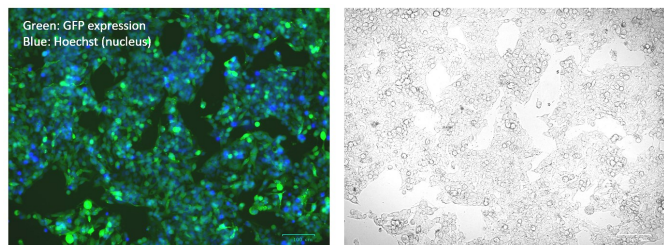
Tunable Size

Batch Consistency

Nucleic Acids LNP Synthesis

Choice of cationic or ionizable lipid
x/LipidFlex = 40/60

High Encapsulation Efficiency

Choice of cationic or ionizable lipid
x/LipidFlex = 40/60

Cell Transfection using GFP mRNA LNP

Green: GFP expression
Blue: Hoechst (nucleus)

Fluorescence Field   Bright Field

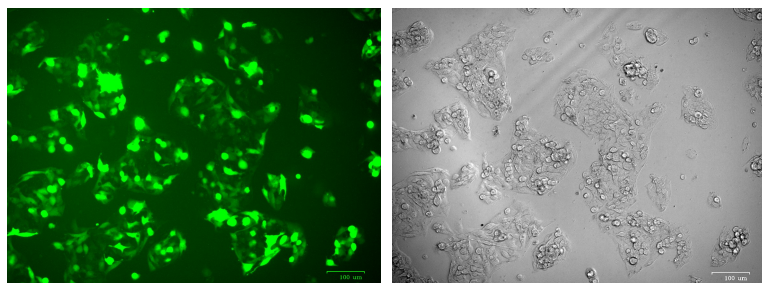| Model	NanoGenerator™ Pro
Mixing Cartridge	CHP-MIX-3
Throughput	2 to 200 mL
Total Flow Rate	4-12 mL/min
Flow Rate Ratio (W:O)	2:1 to 5:1
Size Range	40 to 200 nm
PDI	0.05 to 0.2
Encapsulation Efficiency	Up to 99%
Payloads	DNA, mRNA, siRNA, protein, small molecules

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![PreciGenome logo]

PreciGenome's NanoGenerator™ applies microfluidic approaches to synthesize nanoparticles in a continuous mode. The system has been widely used in the drug delivery field for a variety of applications, such as synthesis of lipid nanoparticles (LNP), liposomes, PLGA, etc.

NanoGenerator™ Max (cGMP version) is designed for clinical and commercial production (100mL-1L, 10L+). With PreciGenome's microfluidics technology, customer can easily and seamlessly transfer their early discovery results (NanoGenerator^{TM} Flex, Pro) to late stage production (NanoGenerator^{TM} GMP).
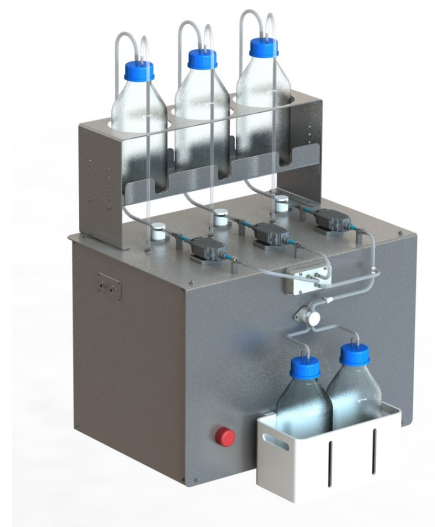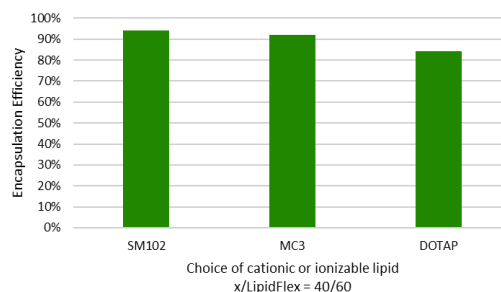
Cell Transfection using GFP DNA LNP

Fluorescence Field   Bright Field

High Encapsulation Efficiency

Model	NanoGenerator^{TM} Max	NanoGenerator^{TM} Max+
Throughput	100mL to 1L	>= 10L
Total Flow Rate	>1L/hour	>10L/hour
Size Range	40 to 200 nm	40 to 200 nm
PDI	0.05 to 0.2	0.05 to 0.2
Encapsulation Efficiency	Up to 99%	Up to 99%
Payloads	DNA, mRNA, siRNA, protein, small molecules	DNA, mRNA, siRNA, protein, small molecules
Inline Dilution	Optional	Optional

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
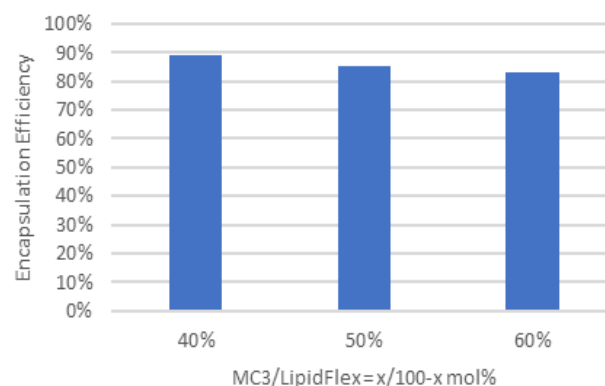- High mammalian cell transfection rate

Model	LipidFlex™	LipidFlex™ Pack
Catalog #	PG-SYN-LF1ML	PG-SYN-LF1MLP
Components	Structural Lipid/Cholesterol/Stabilizer	SM102/Structural Lipid/Cholesterol/Stabilizer
Product size	1000 μL	1000 μL
LipidFlex Conc.	30 mM	30 mM
Ionizable lipid	NA	SM102 (20mg)

Size & PDI
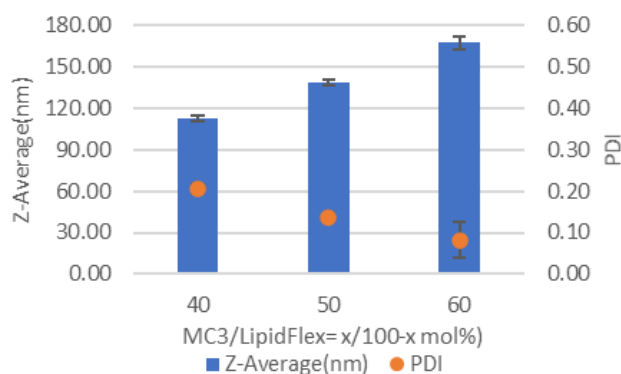
Encapsulation Efficiency

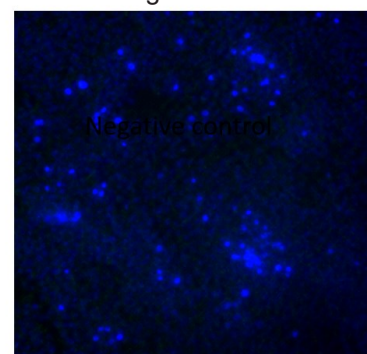### LipidFlex™ Pack Kit Experiment: HepG2 Cell Transfection Efficiency
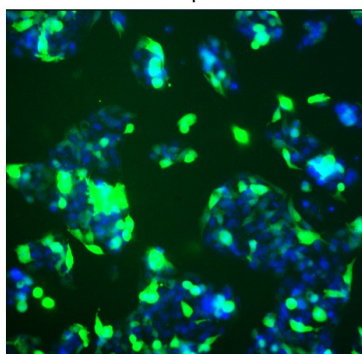
| Sample	Positive control	Negative control
DNA LNP, PreciGenome NanoGenerator SM102/PG-LipidFlex = 40/60 mol%	Lipofectamine™ 3000 (Thermo Fisher)	Non-treat
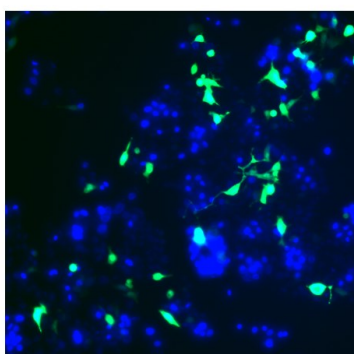
LipidFlex™ T Cell Kit

High Efficient mRNA LNP Formulation for T Cell Transfection

LipidFlex^{TM} T cell kit is a high efficient lipid formulation to synthesize mRNA lipid nanoparticles for primary human T cell gene delivery. Using NanoGenerator^{TM} Flex-S system and CHIP-MIX-4 cartridge, customers can prepare potent mRNA LNP in a convenient and efficient way.
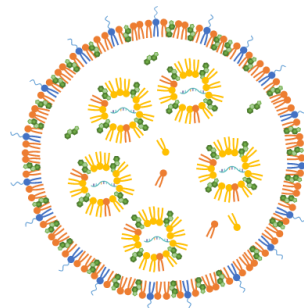
- Narrow size distribution of mRNA LNP

- High transfection efficiency

- High protein expression level

- High cell viability

- Time efficient synthesis process

Component	Size	Storage
LipidFlex T Lipid mix	200 μL	-20 ℃
Formulation Buffer 1 (10x)	60 μL	4 - 8 ℃
Formulation Buffer 2	1 mL	4 - 8 ℃

Customer Service

- **Formulation design (Lipid NP, Liposome or PLGA)**

    Customize liposomes design based on our clients' demand by varying lipid compositions, vesicle sizes, surface charges, etc.

- **Payload encapsulation**

    Customize protocols to encapsulate drug molecules into lipid nanoparticle or PLGA with high encapsulation efficiency.

- **Cell study**

    Cell in vitro transfection service.

- **Analysis and characterization**

    Run comprehensive analysis assays for liposomes before and after encapsulation, which includes visual appearance, size distribution, stability, entrapment efficiency, encapsulation efficiency analysis, in vitro release profile analysis, release rate, etc.

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Ordering Information

Platforms		
NanoGenerator^{TM} Flex-S	NanoGenerator^{TM} system, throughput: 0.2mL-1mL	PG-SYN-FS
NanoGenerator^{TM} Flex-M	NanoGenerator^{TM} system, throughput: 1mL-12mL	PG-SYN-FM
NanoGenerator^{TM} Flex	NanoGenerator^{TM} system, throughput: 0.2mL-12mL, S and M module	PG-SYN-F
NanoGenerator^{TM} Pro	NanoGenerator^{TM} system, throughput: 2mL-50mL, integrated instrument	PG-SYN-P
NanoGenerator^{TM} Max	GMP version nanoparticle synthesis system (available soon)	PG-SYN-G
Microfluidic Cartridge & Consumables		
Mixing cartridge	Microfluidic mixing chip for Flex, 4 devices per chip	CHP-MIX-4
Mixing cartridge	Microfluidic mixing chip for Pro, 3 devices per chip	CHP-MIX-3
Mixing cartridge	Microfluidic glass mixing chip for Flex-M, 1 device per chip	CHP-MIX-G1
Reservoir Connectors	Reagent Reservoirs for Flex-S, 20sets/pack	PG-MRC-SYNS-Q20
Flex-S Gasket	Gaskets for Flex-S, 20pcs/pk	PG-GSK-SYNS-Q20
O-ring Gasket	O-ring gasket for NanoGenerator^{TM} Pro, 50pcs/pk	PG-ORN-SYNP-Q50
Reagents (optional)		
LipidFlex^{TM} kit	3 components lipids mixture, 1mL	PG-SYN-LF1ML
LipidFlex^{TM} Pack kit	Pack of LipidFlex^{TM} and ionizable lipid (SM102)	PG-SYN-LF1MLP
LipidFlex^{TM} T cell kit	T cell transfection kit	PG-SYN-LFT
LipidDemo	Included in the package of the instrument	PG-SYN-LFD
Accessories & Service (optional)		
Flex-S flow unit	Flow unit for Flex-S	PG-SYN-MNTS
Flex-M flow unit	Flow unit for Flex-M	PG-SYN-MNTM
Tubing and connector kit	Standard tuning and connectors for Flex-M	KIT-TUB-FIT-FM
Inline dilution kit	Inline dilution device, tubing and connectors for Flex-M	KIT-INL-DIL-FM
Extended Warranty	1 to 3 years.	PG-WTY-1Y

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 since we started our business. Our technology enables rapid prototyping with high quality and reliable performance for lipid nanoparticles, liposomes, PLGA, etc.

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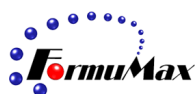Tel: 86-512-67503398
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