迈安纳®
Micro&Nano

Rapid Nanomedicine System

—Make mRNA therapy development easier!

- mRNA-LNP
- mRNA Vaccine
- CAR-T
- CRISPR-Cas9
- Protein Substitution Therapy
- Small Molecule Drugs

About US

16+
IND & EUA

20+
patents

300+
service

- Micro&Nano Biologics Co.,Ltd., founded in 2018, focusing on providing integrated mRNA delivery solutions to the sore points of RNA industry.
- The company not only provides a full range of RNA-LNP encapsulation equipment (including mRNA, siRNA, CRISPR/Cas9, SAMRNA, CircRNA, etc.) from the laboratory to industrialization, but also offers overall solutions.
- Numerous users have obtained over 13 IND clinical trial approvals through the use of the INano platform in China, the United States, Brazil, Australia and other countries.

Overall solutions focused on nanomedicine

DNA — mRNA — miRNA — siRNA — saRNA — Circle RNA — CRISPR Cas9

Experience: **Micro&Nano** has provided standard and customized nucleic acid drug delivery equipment and solutions to hundreds of companies and research institutions, with carrier types including LNP, polymer core-shell, PLGA, peptides, liposomes, nanocrystals, and other various types.

Quality: **Micro&Nano's** solutions can effectively control the size of nanoparticles, increase encapsulation efficiency, and have good repeatability in the preparation process, with low PDI values for product performance between batches and groups. This simplifies the overall experimental process and improves the preparation process, which can be linearly amplified through our unique Genmix™ technology.

Technology: **Micro&Nano** is committed to developing customized nucleic acid drug delivery solutions using its leading proprietary Genmix™ technology. Customized equipment and solutions are developed based on customer needs and different carrier characteristics to meet the requirements of research and GMP production.

Service: **Micro&Nano** always prioritizes product and service quality, and has an experienced engineering team, GMP consulting team, and technical application team. A single batch production line can reach over 100 liters, which helps in the conversion of nanomedicine from early-stage research to clinical products and commercial production.

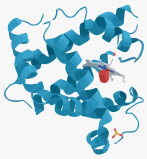
Nano Drug Delivery Systems

- Drug nanocarriers/nanocarrier drugs/nano drug delivery systems are carriers with particle sizes ranging from 10 to 1000 nm that encapsulate active pharmaceutical ingredients (APIs) for in vivo delivery. They can effectively regulate the release rate of drugs, increase the ability of drugs to penetrate biological membranes, change the in vivo distribution of drugs, and improve their bioavailability.
- It can be used for the delivery of a series of APIs :RNA, DNA, CRISPR, protein, small-molecule targeted drugs, contrast agents, etc., realizing the integration of diagnosis and treatment.

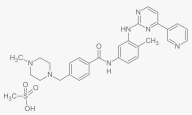
RNA

DNA

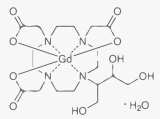
CRISPR



PROTEIN

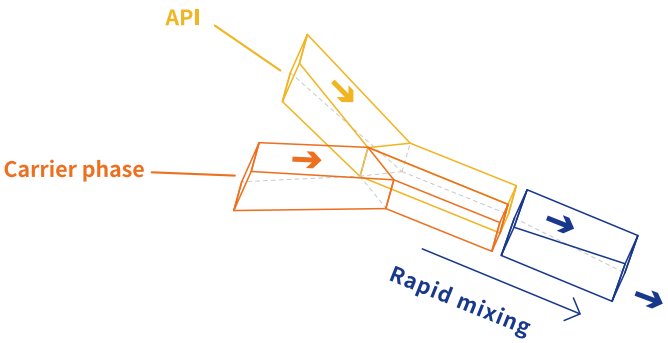


Small molecule targeted drugs



Contrast Agent

Genmix™ Technology



- Carrier phase and API flow into the Cartridge
- The unique patented "Counter-Swirl Vortex" micro-mixing technology.
- It achieves precise and ordered mixing, causing rapid changes in liquid polarity, which triggers the self-assembly of nanoparticles to encapsulate drugs.

* The nano drug manufacturing system utilizes Genmix™ technology to rapidly self-assemble nanoparticles, nanoliposomes, polymer nanoparticles, and other materials suitable for encapsulating active pharmaceutical ingredients such as nucleic acids, small molecules, peptides, or proteins.

Advantages of INano™ Platform

- Rich practical experience in the manufacturing of nucleic acid drugs, which has provided services to hundreds of domestic customers, supporting multiple types of delivery carriers, including but not limited to LNP, polymers, peptides, liposomes, and PLGA.
- We have independently developed Genmix™ technology, which enables linear scale-up to an industrial level with minimal risk and material cost.
- We offer highly customized equipment and optimized process flow based on the unique characteristics of your delivery vehicles,providing personalized customization.

Rapid Nanomedicine System

INano™E

Formulation screening

1

- 0.4-20ml preparation volume
- Rapid screening of prescription
- Sterility, enzyme-free and pyrogen-free of Cartridge
- Temperature control
- Compatible with various brands of syringes
- The Cartridge has no limit on the number of uses
- 0.1-30ml/min flowrate, Multiple mixing structures (chaotic flow, cross flow, T-mixing, etc) available, various mixer materials available.

INano™L/L+

Formulation screening
& scale-up process screening

2

- 0.4-20mL preparation volume (0.4-60mL preparation volume)
- Rapid screening of prescription
- Sterility, enzyme-free and pyrogen-free of Cartridge
- Temperature control
- Compatible with various brands of syringes
- The Cartridge has no limit on the number of uses
- 2 in 1, supports both Formulation screening & scale-up process screening simultaneously.
- 0.1-150ml/min(0.1-300ml/min) flowrate, Multiple mixing structures (chaotic flow, cross flow, T-mixing, etc) available, various mixer materials available.

INano™P(cGMP)-customizable

IND/Clinical/ GMP manufacture

3

- Unique process technology，waste ＜ 20mL
- Highly automated, capable of automatic exhaust and automatic switch-ingr waste liquids.
- Multiple modules are available （flow sensor，On-line DLS）
- Multiple mixing structures (chaoticflow, cross flow, T-mixing, etc) available, various mixer materials (eg., Henschelalloy) available.
- Complete biocompatibility research data on contact materials
- Production capacity: from 100ml to several tens of liters.
- Provide equipment GMP validation activities and documentation support
- Equipments complies with cGMP production requirements and t FDA 21CFR Part 11 requirements

INano™S(cGMP)-customizable

cGMP large-scale production

4

- Complete process solution
- Production capacity：⩾2L/min（without dilution）
- Highly automated, capable of automatic exhaust and automatic switchingr waste liquids
- Multiple mixing structures (chaoticflow, cross flow, T-mixing, etc) available, various mixer materials (eg., Henschelalloy) available.
- Complete biocompatibility research data on contact materials
- Equipments complies with cGMP production requirements and t FDA 21CFR Part 11 requirements

Core Advantages

New design reduces the risk of mRNA degradation

High reproducibility and higher production capacity

Complete biocompatibility research data

Data integrity complies with 21CFR Part 11

Recordable and traceable

Remote diagnostics, upgrades and technical support

Integrated NanoSmart ® laboratory method

GenNano™ Platform

- GenNano™-LNP-mRNA is a reagent combination used for the rapid and convenient preparation of LNPs (lipid nanoparticles) for mRNA delivery. It contains a solution of ionizable cationic lipid mixture and RNA dilution buffer. By using microfluidic technology under certain conditions, the ionizable mixture and nucleic acid can be mixed to form GenNano™-LNP, which can be used as an evaluation tool for in vitro and in vivo effects of nucleic acid raw materials by customers

LNP-mRNA kit

Carrier type: LNP
(lipid nanoparticles)

Features

- It can encapsulate mRNA
- 95% transfection efficiency
- Hypotoxicity
- Complete protocol available

LNP-siRNA kit

Carrier type: LNP
(lipid nanoparticles)

Features

- It can encapsulate siRNA
- High transfection efficiency
- Hypotoxicity
- Complete protocol available

LNP-T Cell kit

Carrier type: LNP
(lipid nanoparticles)

Features

- It can encapsulate mRNA siRNA, CRISPR/Cas9 and other nucleic acids
- High transfection efficiency of T cells
- Hypotoxicity
- Complete protocol available

Notes: Only for scientific research purposes, not for human clinical trials

Service

Discussion, signing of contracts and confidentiality agreements →

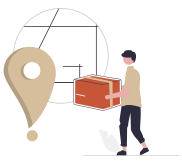
Customer's sample Preparetion →

Sample delivery to Micro & Nano →

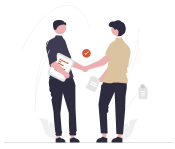
RNA drugs are encapsulated (mRNA, siRNA, CRISPR/Cas9)

Downstream processing ←

Analysis and testing ←



Final products delivery to customer with full report ←

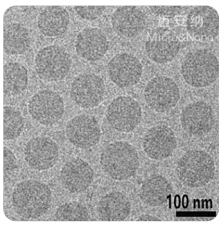


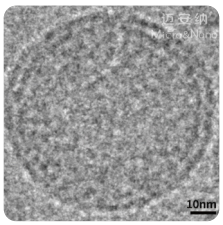
End of service

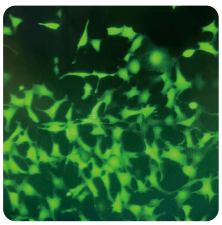
Data

Micromorphology and transfection efficiency

- Typical LNP structure observed under electron microscopy, almost 100% cell transfection efficiency.







From Zhejiang University, PRC

INano L

+

Cartridge

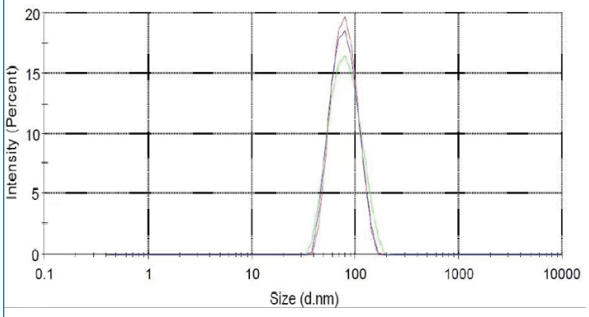
12ml/min

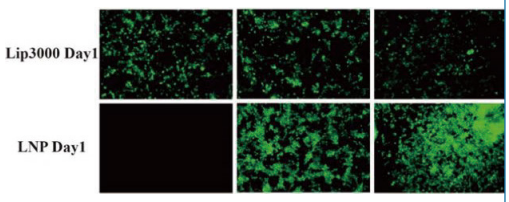
LNP used in delivery of EGFP mRNA

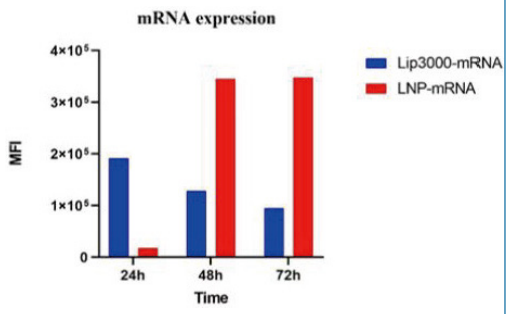
- Uniform and stable particle size, high cell transfection efficiency

Record	Sample Name	Z-Average (d.nm)	Polymer dispersity index(PDI)	zeta potential
		d.nm		mV
1		74.62	0.079	1.08
2		74.57	0.097	0.709
3		73.51	0.083	-0.785
Mean 1-3		74.23	0.086	0.335

Size Distribution by Intensity







Size: 74.23 nm; PDI: 0.086; Zeta Potential: 0.335 mV

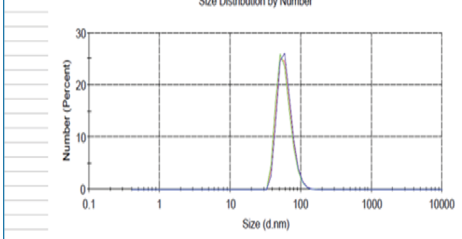
12ml/min

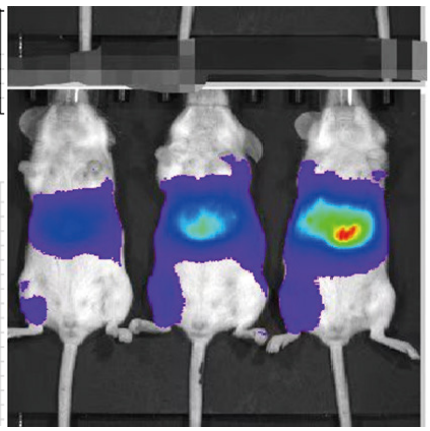
LNP used in delivery of Luciferase mRNA

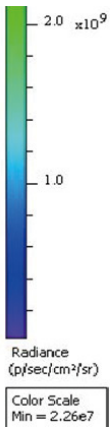
- Uniform and stable particle size, good expression effect in vivo

Record	Sample Name	Z-Average (d.nm)	Poly dispersity index (PDI)	Zeta Potential (mV)
1		80.72	0.091	0.0207
2		79.94	0.088	0.164
3		78.64	0.067	-0.306
Mean 1-3		79.73	0.08	-0.04

Size Distribution by Number



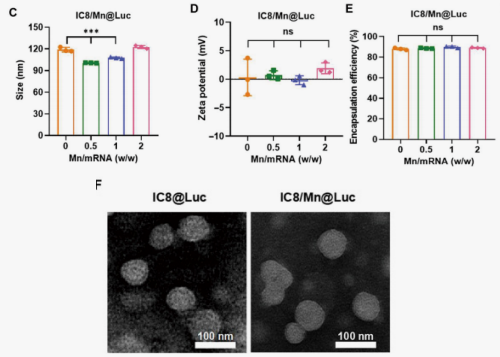




Size: 79.73 nm;PDI: 0.08; Zeta Potential: -0.04 mV

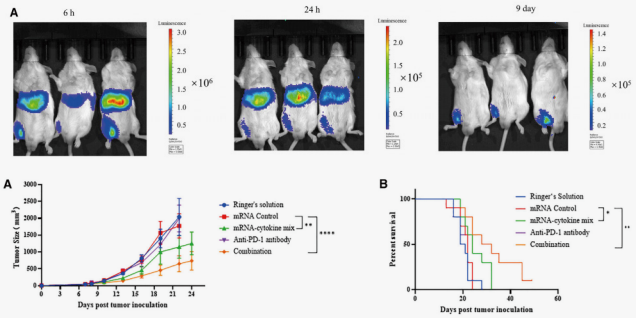
Publication

• Uniform morphology and high encapsulation rate



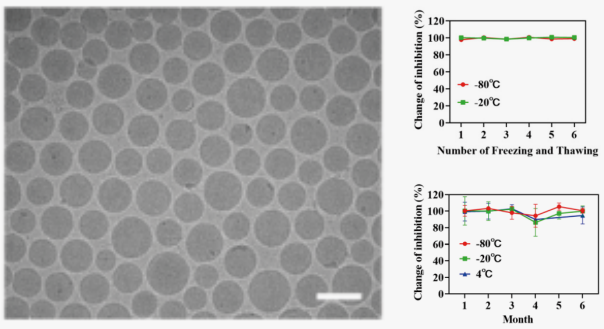
Fan et al. Science Advances. 2022, 8, eabq3500.

• Long-lasting mRNA expression/effective tumor inhibition effect in vivo



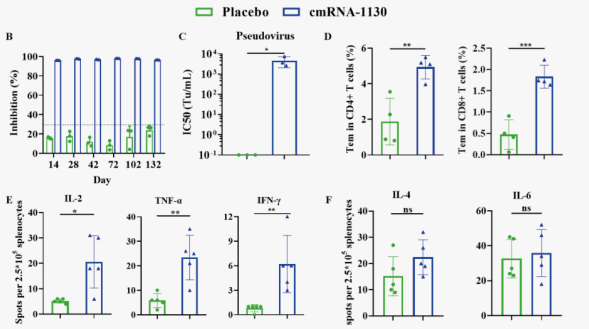
Ren et al. Signal Transduction and Targeted Therapy. 2021, 6, 213.

• Good stability



Huang et al. bioRxiv. DOI: 10.1101/2022.05.12.491597.

• Strong immunological effect



Huang et al. bioRxiv. DOI: 10.1101/2022.05.12.491597.

Publications by customers

1. Yang, R et al. A core-shell structured COVID-19 mRNA vaccine with favorable biodistribution pattern and promising immunity. Signal Transduction Target Therapy. 2021, 6: 213. https://doi.org/10.1038/s41392-021-00634-z

2. Yang, Jiali et al. Intratumoral delivered novel circular mRNA encoding cytokines for immune modulation and cancer therapy. Molecular Therapy - Nucleic Acids. 2022, 30: 184-197. https://doi.org/10.1016/j.omtn.2022.09.010

3. Huang, Ke et al. Delivery of Circular mRNA via Degradable Lipid Nanoparticles against SARS-CoV-2 Delta Variant. bioRxiv 2022. https://doi.org/10.1101/2022.05.12.491597

4. Mao, Shanhong et al. A highly efficient needle-free-injection delivery system for mRNA-LNP vaccination against SARS-CoV-2. Nano Today. 2023, 48: 101730. https://doi.org/10.1016/j.nantod.2022.101730

5. Fan, Na et al. Manganese-coordinated mRNA vaccines with enhanced mRNA expression and immunogenicity induce robust immune responses against SARS-CoV-2 variants. 2022, 8 (51): eabq3500. https://doi.org/10.1126/sciadv.abq3500

6. Shen, Zhigao et al. Development of a Library of Disulfide Bond-Containing Cationic Lipids for mRNA Delivery. Pharmaceutics. 2023; 15 (2): 477. https://doi.org/10.3390/pharmaceutics15020477

7. Zhang et al. Algorithm for Optimized mRNA Design Improves Stability and Immunogenicity. **Nature** (2023). https://doi.org/10.1038/s41586-023-06127-z

8. Su et al., A Quadrivalent mRNA immunization elicits potent immune responses against vaccinia and monkeypox viral antigens – a step closer to a broad orthopoxvirus vaccine. bioRxiv. https://doi.org/10.1101/2023.04.23.537951

9. Wang et al. Strong immune responses and protection of PcrV and OprF-I mRNA vaccine candidates against Pseudomonas aeruginosa. npj Vaccines. 2023, 8: 76. https://doi.org/10.1038/s41541-023-00672-4

10. Miao et al. Optimization of formulation and atomization of lipid nanoparticles for the inhalation of mRNA. International Journal of Pharmaceutics. 2023, 640: 123050. https://doi.org/10.1016/j.ijpharm.2023.123050

11. Xia et al. Mpox virus mRNA-lipid nanoparticle vaccine candidates evoke antibody responses and drive protection against the Vaccinia virus challenge in mice. Antiviral Research. 2023, 105669. https://doi.org/10.1016/j.antiviral.2023.105668

迈安纳® Micro&Nano

+86 2154281913

Micro&Nano Biologics Co.,Ltd.

info@micronanobiologics.com

www.micronanobiologics.com

Building A, No. 128 Shenfu Road, Minhang District, Shanghai，China