Scalable mRNA-LNP Manufacturing Enabled by Microfluidic In-Line Dilution Across Development and Production Scale

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Novel Microfluidic DDS Platform
Inventage Lab

Background

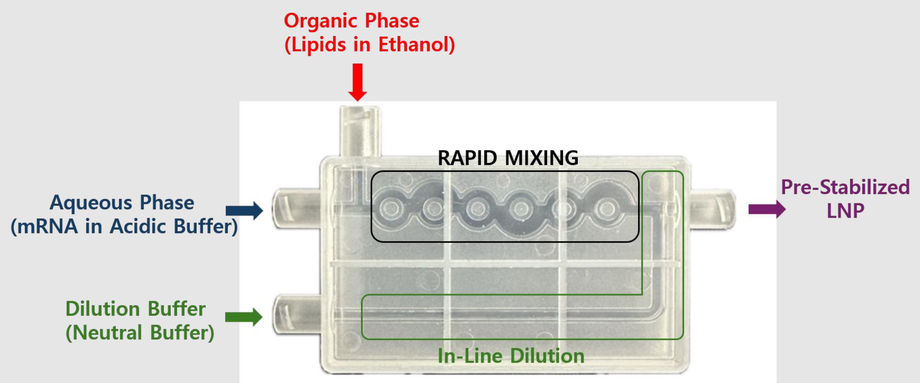
The Scalability Challenge in RNA-LNP Manufacturing
: Long processing times, Batch-to-batch variability, Limited scalability, Loss of critical quality attributes (CQAs)

Solution

IVL-GeneFluidic® Platform; Gene-to-GMP Manufacturing
: Proprietary microfluidic mixing and rapid in-line dilution technology

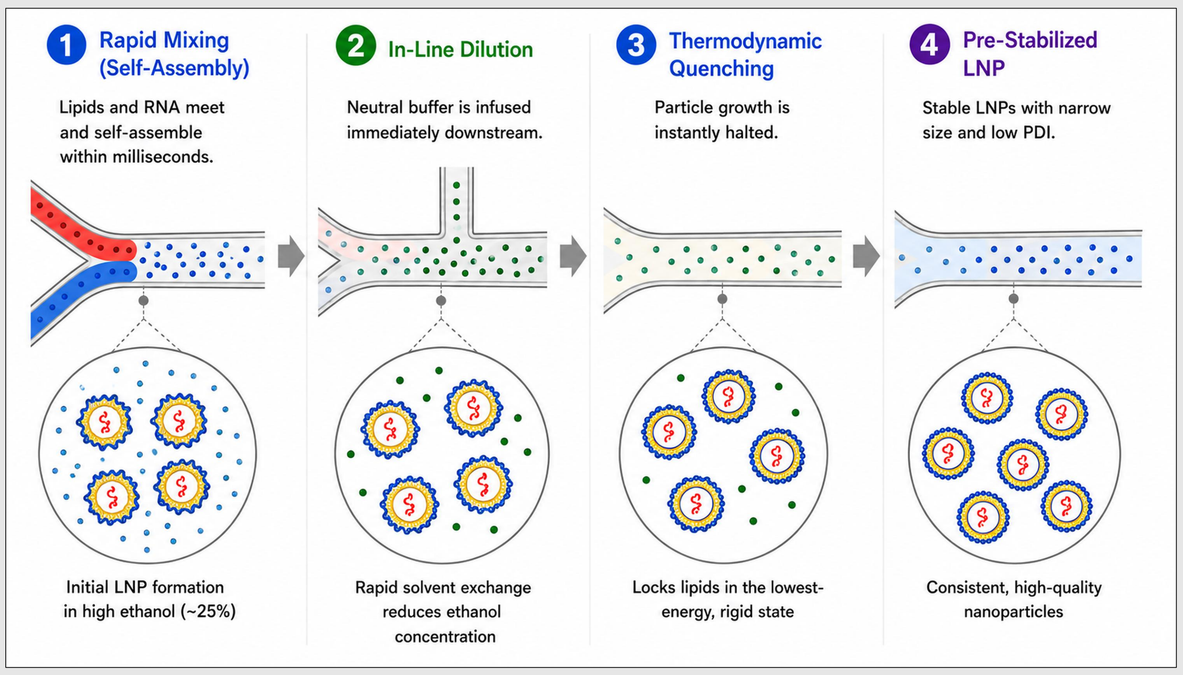
Method

Ⅰ. Controlled Self-Assembly Through In-Line Dilution



❖ **Precision Fluidic Engineering**

: This enables reproducible nanoparticle nucleation, uniform particle growth, and consistent CQAs across manufacturing scales.



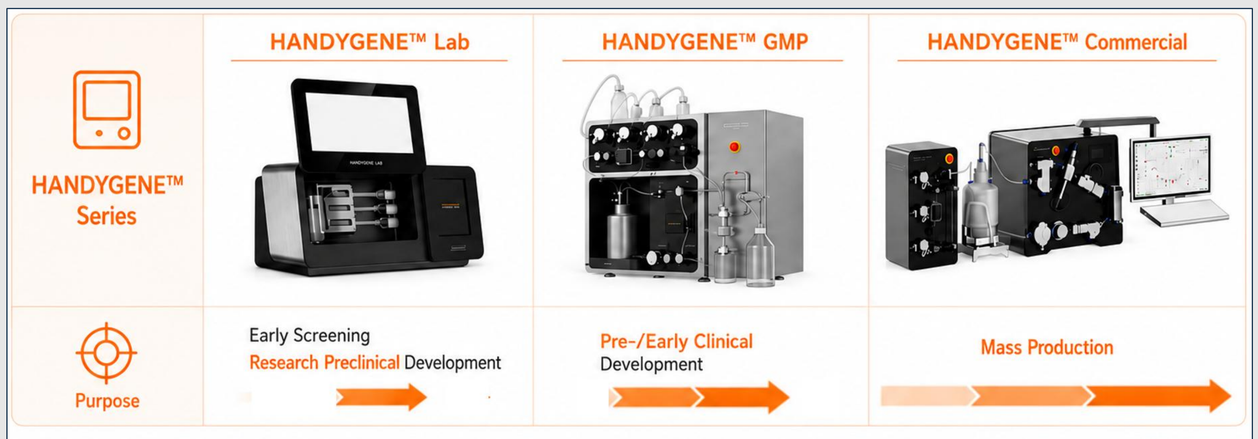
❖ **Thermodynamic Quenching by In-Line Dilution**

: This rapid solvent exchange reduces local ethanol concentration, restores pH level within milliseconds and stabilizes LNP structure at its thermodynamic minimum-energy state.

Ⅱ. Scale-Independent Manufacturing

❖ **Consistent LNP Quality Across Manufacturing Scales**

: **The HANDYGENE™ platform** enables scale-independent manufacturing by maintaining equivalent fluidic assembly conditions across laboratory, GMP, and commercial production systems.



	LNP Formulation Equipment	Post-treatment method	mRNA amount per batch (mg)	Total flow rate (mL/min)	Size (nm)	PDI	Yield (%)
	HANDYGENE™ LAB	Dialysis and Centrifuge	0.1	8	62.4	0.07	< 70
	HANDYGENE™ GMP	Tangential flow filtration	16	250	67.7	0.04	78.0
	HANDYGENE™ Commercial	Tangential flow filtration	100	500	67.5	0.03	89.0

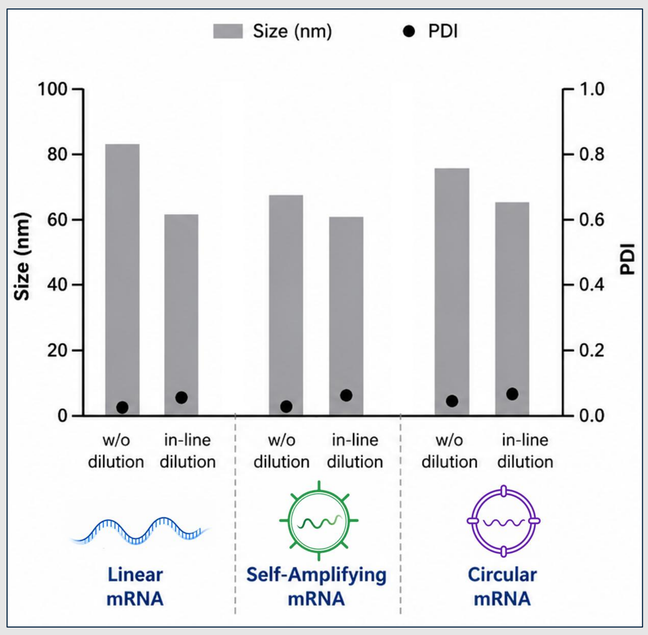
❖ **Fluidic Stabilization Enables Integrated TFF Processing**

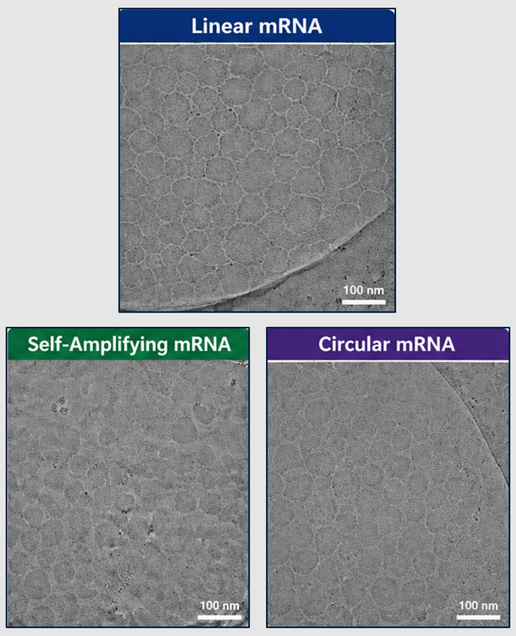
: The IVL-GeneFluidic® in-line dilution process rapidly stabilizes nanoparticles immediately after self-assembly, producing mechanically robust LNPs capable of tolerating continuous TFF purification.

One Process. One Platform. Any Scale.

Result

Ⅰ. Versatility Across RNAs





❖ **Payload Independent LNP Manufacturing**

: **The IVL-GeneFluidic® platform** minimizes payload-dependent variability, enabling reproducible LNP formation regardless of RNA modality.

One Process. One Platform. Any RNA.

Ⅱ. Preserved Biological Performance After Scale-Up

Figure 1. Equivalent Immunogenicity Across Manufacturing Scales

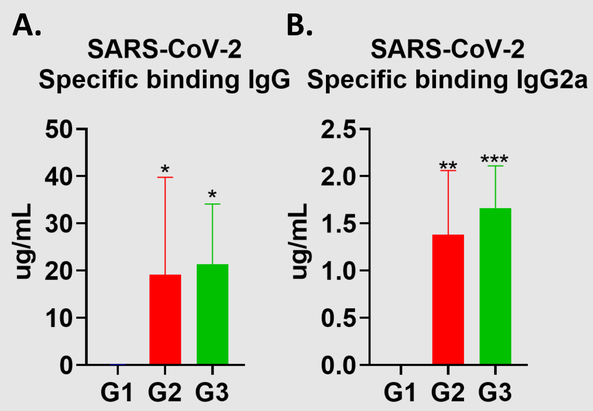
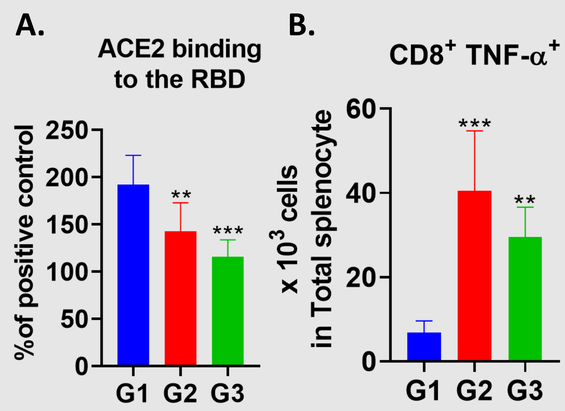


Figure 2. Functional Neutralization and Cellular Immunity



G1 = Control, G2 = 30 mL scale + Centrifuge, G3 = 3.6 L scale + TFF
(1st dose = week 0, 2nd dose = week 3, Peak analysis = week 5)

Conclusion

One Process. One Platform. Any RNA, Any Scale.

The IVL-GeneFluidic® platform enables payload-independent and scale-independent RNA-LNP manufacturing through controlled self-assembly and in-line dilution, providing a seamless pathway from laboratory development to GMP and commercial production.

References
[1] Lai G. et al, Biophys Chem., 2015, [2] Carvalho BG. et al, Pharmaceutics, 2022.,
[3] Giovanni Bovone et al, Macromolecules, 2022, [4] Jiwoo Hong et al, ACS Appl. Mater. Interfaces, 2024

Acknowledgements
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