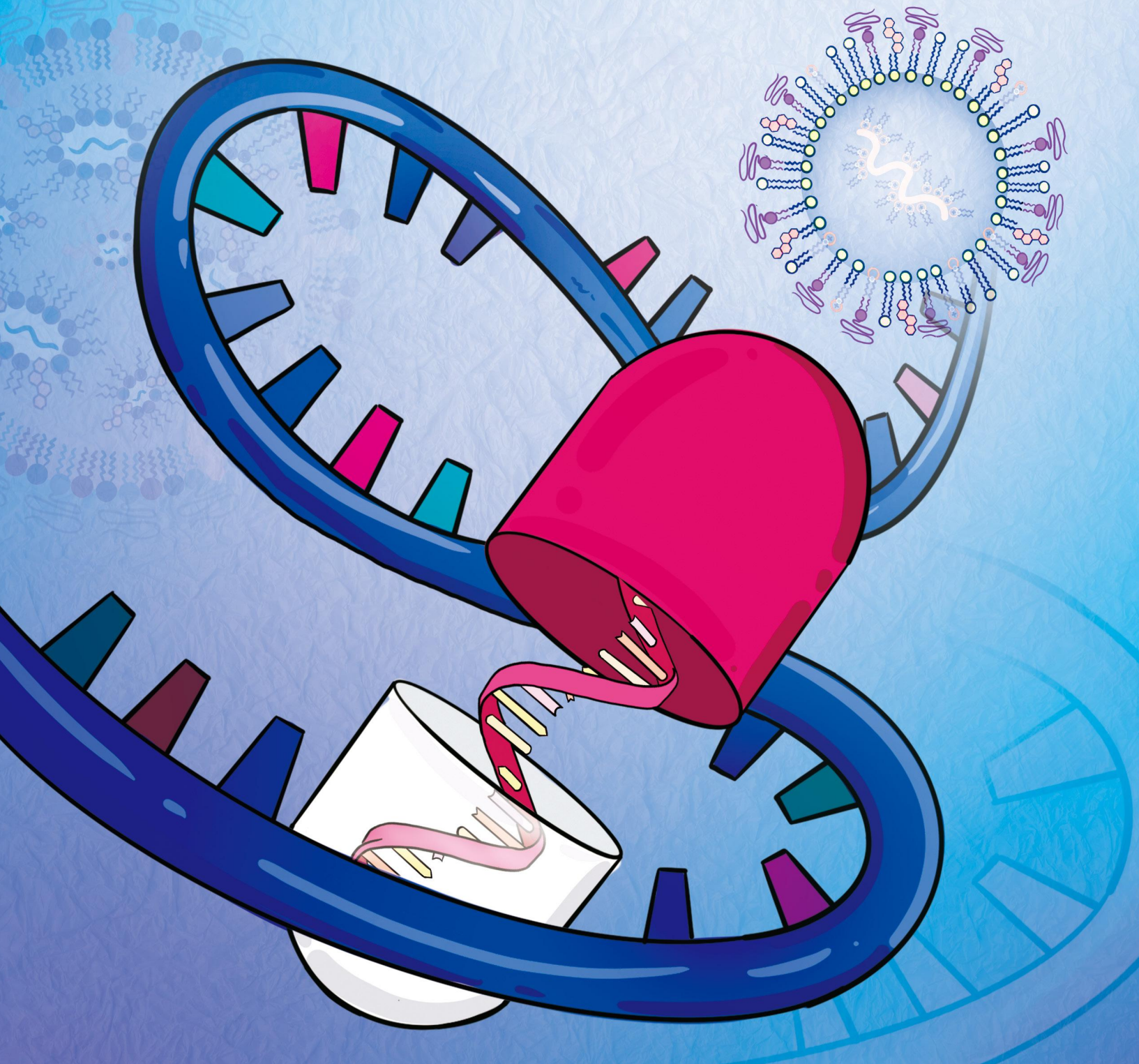
VectorBuilder
Revolutionize Gene Delivery

RNA

from Design to Therapy



VectorBuilder

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About VectorBuilder

As a global leader in gene delivery technologies, VectorBuilder offers a full spectrum of gene delivery solutions covering virtually all research and clinical needs from basic research to therapy. We have supported thousands of laboratories and biotech/pharma companies across the globe along their entire drug-discovery pipelines, going from research-grade vectors for early discovery, to GMP-like vectors for preclinical testing, to full GMP-grade vectors for clinical trials. Our four major business segments include research vectors & viruses, gene delivery CRO services, CDMO services, and IP out-licensing.

VectorBuilder's Four Major Offerings

Research Vectors & Viruses

- Vector design & cloning
- Plasmid DNA preparation
- Virus packaging

Gene Delivery CRO Services

- Library construction & screening
- Stable cell line engineering
- Therapeutic IVT RNA development
- AAV capsid evolution in NHP
- AAV biodistribution in NHP
- Promoter engineering/screening
- BAC recombineering

CDMO Services

- Plasmid GMP manufacturing
- Viral vector GMP manufacturing (AAV,LV,MMLV,etc.)
- IVT RNA and LNP manufacturing
- Cell banking
- Process development & analytical development
- Fill/Finish

IP Out-licensing

- Novel AAV capsids
- Novel tissue-specific promoters
- Experimentally codon-optimized genes
- Virus producer cell lines

VectorBuilder has developed extensive in-house capabilities in method development and analytical testing to ensure the highest quality of IVT RNA, which allows us to consistently exceed customer expectations. Our rigorous documentation practices empower the production of RNA drugs that align with regulatory standards. By partnering with our GMP experts, you can seamlessly transition from discovery and development to clinical RNA drug manufacturing.

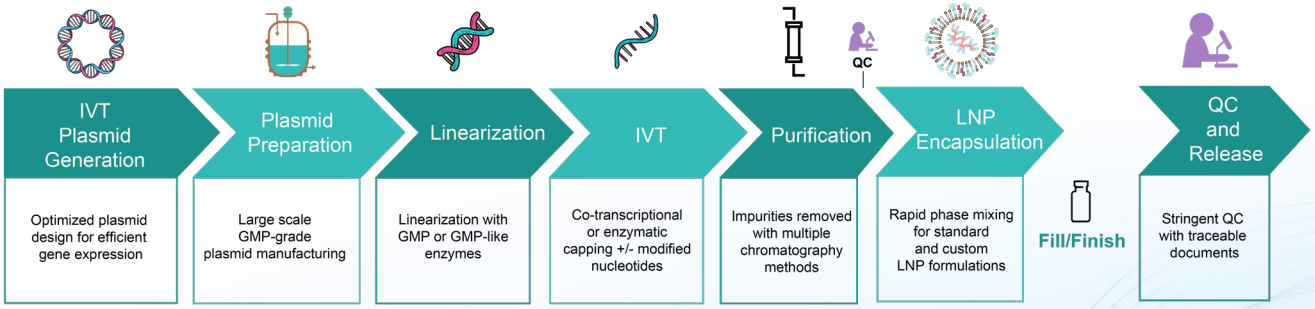
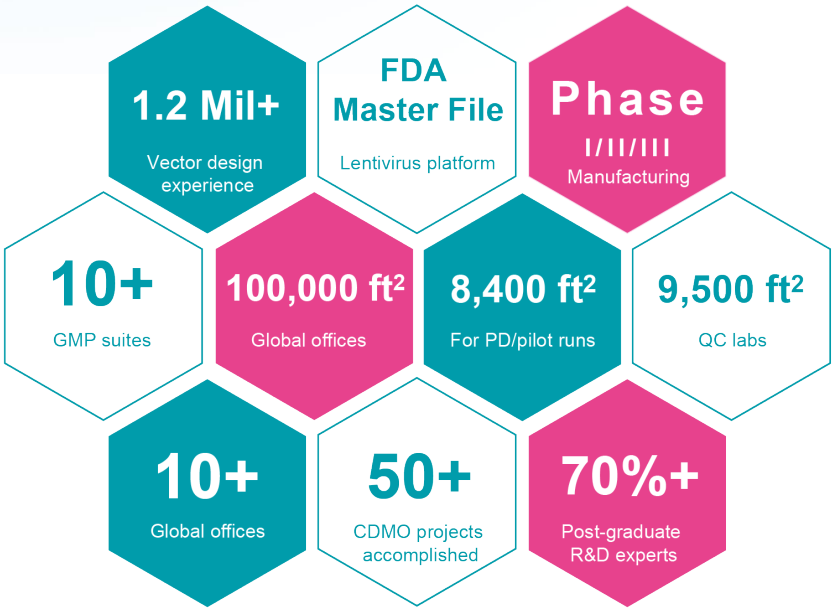


Figure 1. Workflow of IVT RNA manufacturing at VectorBuilder.

VectorBuilder

Our RNA Manufacturing Capabilities

Within our current infrastructure, we facilitate process development, custom IVT RNA synthesis, and GMP-like RNA manufacturing. Our suite of analytical services ensures comprehensive RNA characterization, encompassing assessments of identity, integrity, purity, safety, potency, and functionality. With our commitment to innovation, we continuously refine our processes to stay at the forefront of RNA technology.



VectorBuilder currently has ~100,000 ft² of modern GMP facilities with advanced designs and state-of-the-art equipment. Anticipated to be launched in the fourth quarter of 2024, our new RNA focused GMP facility has been meticulously designed to facilitate the seamless progression of RNA from its discovery phase to clinical drug manufacturing. The design of our facilities prioritizes flexibility and adaptability to cater to custom project requirements.

Our comprehensive facilities include:

- Over 10 GMP manufacturing suites
- Fill/Finish suites
- Quality control laboratories
- Analytical development suites
- Process development suites
- GMP warehouse

Therapeutic IVT RNA

VectorBuilder offers a comprehensive platform for the development of RNA therapeutics including vaccines, gene replacement, chimeric antigen receptor (CAR), and gene editing. Leveraging our extensive design and production experience with premade and custom RNAs, our team can support in vitro transcription (IVT) RNA synthesis and lipid nanoparticle (LNP) encapsulation for a variety of RNA-based expression systems. Researchers can accelerate the development of their RNA therapeutics with our CRO services, offering in vitro and in vivo candidate screening and functional testing.

Highlights

Comprehensive Platform

Offering research and clinical grades of RNA, a variety of RNA systems, customizable IVT RNA production and LNP encapsulation, and a full suite of CRO and CDMO services

Experts in RNA Development

Our team comprises scientists with expertise of the full scope of considerations for therapeutic IVT vector design, sequence optimization and screening, and process development

Highest Quality and Consistency

State-of-the-art facilities and equipment providing the highest purity and consistency, ensured by a full panel of quality control assays

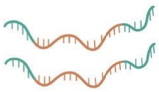
Services Offered

Therapeutic IVT RNA Development

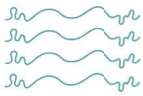
LNP Encapsulation

GMP Manufacturing

Products Offered

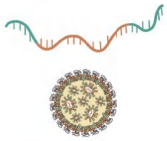


mRNA



saRNA

circRNA



Premade IVT RNA and LNP-RNA

Therapeutic IVT RNA Development

VectorBuilder offers comprehensive CRO services for the development of RNA therapeutics including vaccines, gene replacement, chimeric antigen receptor (CAR), and gene editing. Our team of experts understand key considerations for therapeutic design and process development, and can utilize their know-how to enhance the efficacy, safety, and manufacturability of RNA drugs.

Figure 1. Workflow for IVT RNA therapeutic production.

IVT Vector Design & Cloning

- Proprietary sequence optimization for optimal expression
- Robust cloning and transcription of 120 nt (and longer) polyA tail

UTR Optimization

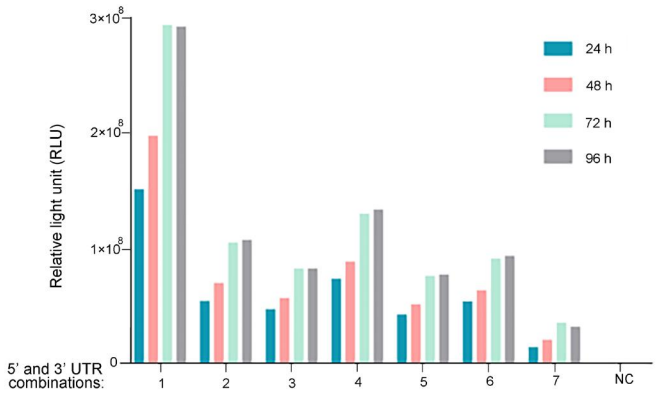


Figure 2. UTR optimization for improved mRNA expression. Different 5' and 3' UTR combinations were tested regulating Gaussia luciferase expression in vitro. HEK293T cells were seeded on 12-well plates at a density of 2.3x10^5 cells per well. Cells were transfected with 1 ug of mRNA per well. At 24 h, 48 h, 72 h, and 96 h post-transfection, Gaussia luciferase activities were measured from cell culture medium.

Coding Sequence Optimization

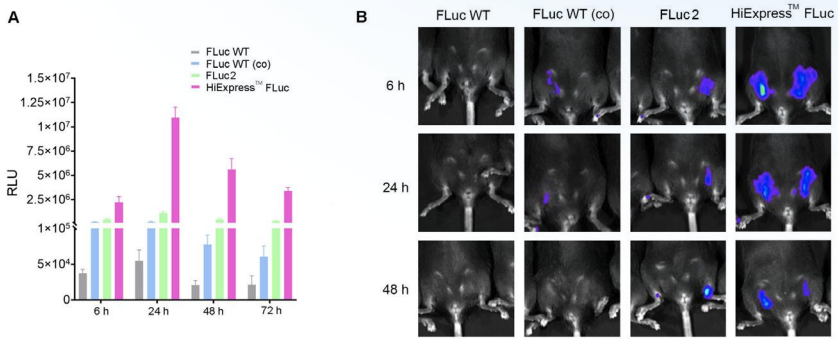


Figure 3. Codon optimization increases mRNA expression in vitro and in vivo. (A) Expression of HiExpress™ Firefly Luciferase mRNA and other luciferase mRNA in HEK293T cells. Cells grown on a 12-well plate were transfected with 0.5 ug of mRNA per well, and luciferase activity was measured at 6 h, 24 h, 48 h, and 72 h post-transfection. (B) Luciferase activity measured in adult C57BL/6 mice injected intramuscularly with 30 ug of LNP-mRNA at 6 h, 24 h, and 48 h post-injection. FLuc WT indicates wild-type firefly luciferase. FLuc WT (co) indicates codon-optimized wild-type firefly luciferase. FLuc2 indicates Luc2 firefly luciferase.

PolyA Integrity

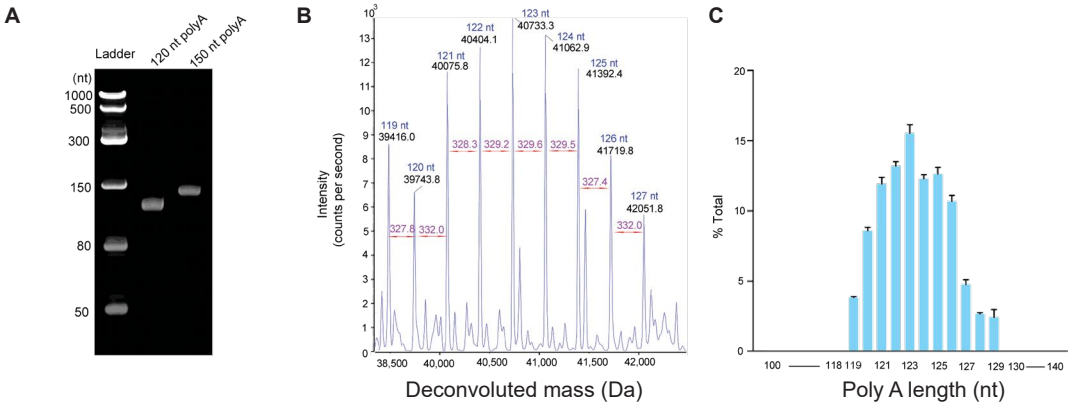


Figure 4. PolyA tail size analysis. PolyA tails were cleaved from IVT mRNA using ribonuclease T1 and isolated by oligo dT affinity chromatography. (A) Isolated polyA tails analyzed by Urea-PAGE gel electrophoresis. (B) Isolated polyA tails analyzed by LC-MS. Deconvoluted spectrum was generated from 120 pmol of polyA tails with an expected size of 120 nt. (C) Size distribution of polyA tails with an expected size of 120 nt. Error bars represent standard deviation from triplicates. Weighted average length is 123 nt.

PolyA Length and GOI Expression

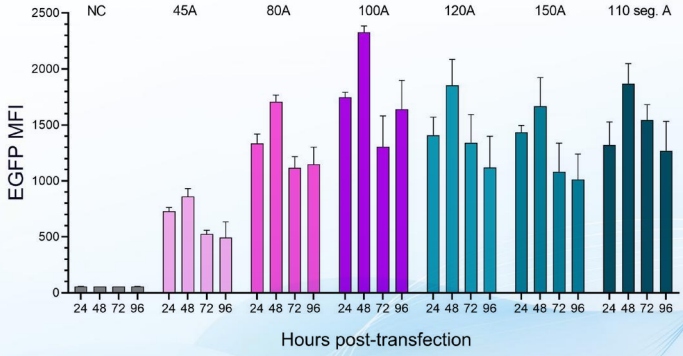


Figure 5. The influence of polyA length and structure on translational efficiency. HEK293T cells were transfected with IVT EGFP mRNA with the same Cap1 and UTRs but different polyA tail lengths as listed above.

IVT RNA Production

- As fast as 5 weeks from vector cloning to LNP encapsulation
- Synthesis of up to 10,000 nt mRNA and saRNA, and 5,000 nt circRNA from microgram (ug) to gram (g) scales
- High capping efficiency (up to 99%) by co-transcriptional or enzymatic methods
- Various modified nucleotide options: m1Ψ, m5C, 5moU, etc.
- Proprietary purification process to efficiently remove impurities
- Comprehensive QC panel
- Cell-free production of IVT template DNA offered that greatly shortens the production time for large-scale IVT RNA manufacturing

mRNA Integrity

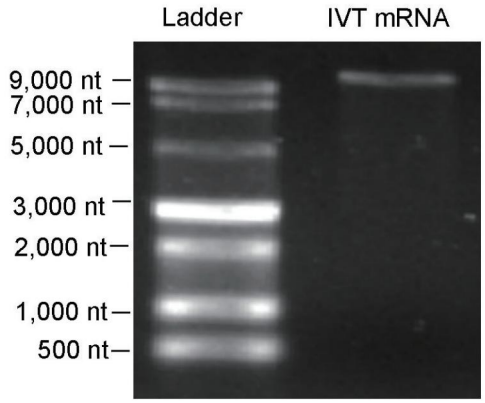


Figure 6. Denaturing agarose gel result indicates high integrity IVT RNA >10,000 nt.

Capping Efficiency

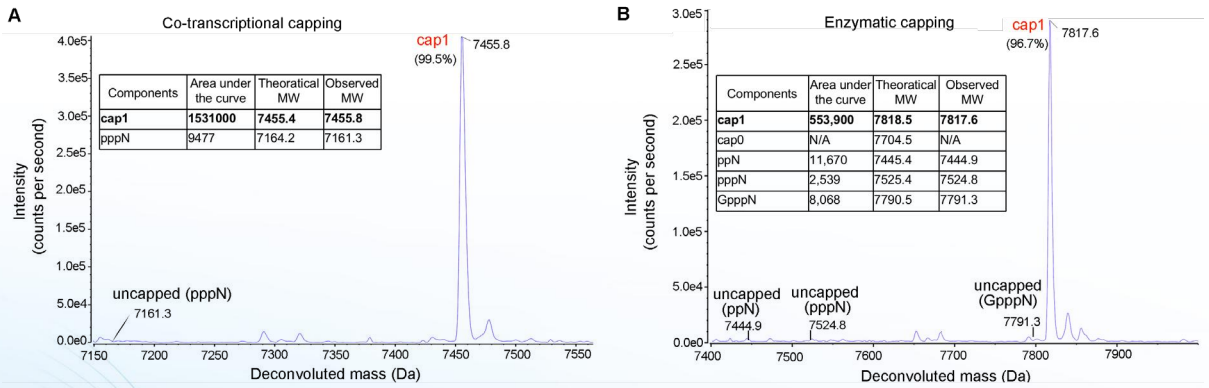


Figure 7. IVT mRNA capping efficiency analyzed by LC-MS. Highly efficient capping (>99%) can be achieved either using (A) co-transcriptional or (B) enzymatic approaches.

Modified Nucleotides

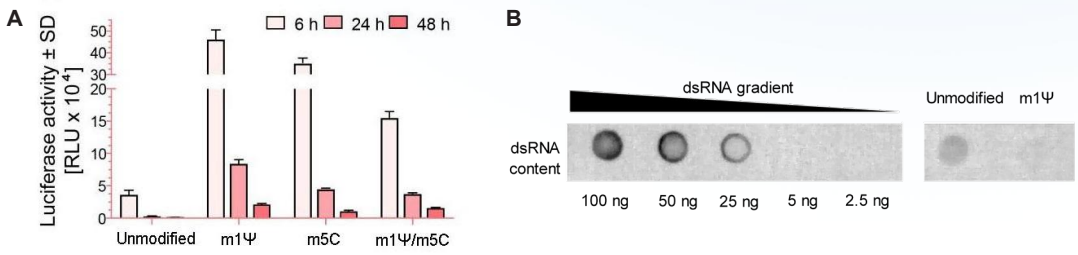


Figure 8. Modified nucleotides increase mRNA expression and decrease dsRNA impurities. (A) Expression of firefly luciferase in HEK293T cells. mRNA was generated with or without modified nucleotides, N1-Methylpseudouridine (m1Ψ) and 5-Methylcytosine (m5C). Cells were grown on 12-well plates and transfected with 1 ug of mRNA per well. Luciferase activities in HEK293T cells at 6 h, 24 h, and 48 h post-transfection were measured. Error bars indicate standard deviations. (B) Equal amounts (750 ng per dot) of magnetic bead-purified EGFP IVT mRNA with or without m1Ψ were assessed by dot blot assay for dsRNA impurities.

dsRNA Removal

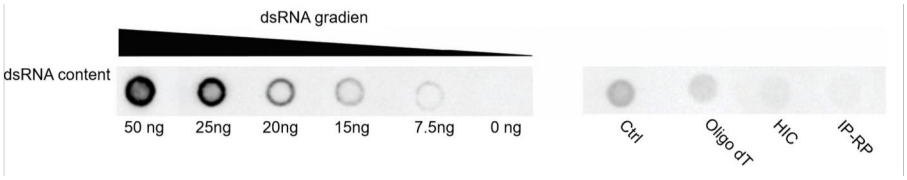


Figure 9. dsRNA removal efficiency of different purification processes. Equal amounts (1500 ng per dot) of hSpCas9 IVT mRNA purified by different processes were assessed by dot blot assay to estimate dsRNA impurities. Abbreviations: HIC, Hydrophobic interaction chromatography; IP-RP, Ion-pair reversed-phase liquid chromatography.

For information on LNP Encapsulation see Page 9.

User Testimonials

> “Amazing experience cooperating with VectorBuilder! As one of the most popular technologies, mRNA vaccine technology has been used extensively to develop therapeutics and vaccines targeting various infectious and non-infectious diseases. Recently, Daniel Meng’s R&D team at VectorBuilder rapidly established the IVT mRNA CRO platform, and we closely collaborated on developing mRNA-based HIV and influenza vaccines. I am so impressed by their scientific vision as well as their problem solving capabilities. Once again, VectorBuilder is trustworthy.”
>
> **Dr. Caijun Sun**
>
> **Sun Yat-sen University, Guangzhou, China**

Quality Control (QC)

VectorBuilder offers an extensive variety of QC methods for IVT mRNA and LNP encapsulation. Default QC items (marked with √) are always performed while optional QC items are performed depending on individual project needs.

Table 1. Quality control services for IVT RNA.

Attribute		QC assay	Research-grade	GMP-like
Identity	mRNA sequence	Sanger sequencing	√	√
	mRNA length	Denaturing agarose gel electrophoresis	√	√
		Capillary gel electrophoresis (CGE)	Optional	√
General/Physical property	mRNA concentration	UV spectrophotometry	√	√
		RiboGreen assay	Optional	√
	Appearance	Visual inspection	Optional	√
Potency	Gene expression	In vitro translation followed by Western blot	Optional	Optional
		Cell transfection	Optional	Optional
Safety	Sterility	Bioburden test	Optional	√
	Mycoplasma	Culture method	Optional	√
		qPCR	Optional	Optional
	Endotoxin	Kinetic chromogenic assay (KCA)	Optional	√
Purity	mRNA integrity	Denaturing agarose gel electrophoresis	√	√
		Capillary gel electrophoresis (CGE)	Optional	√
	A260/280	UV spectrophotometry	√	√
	Capping efficiency	LC-MS	Optional	√
	PolyA analysis	LC-MS	Optional	√
	Residual dsRNA	Dot blot assay	Optional	√
	Residual plasmid DNA	qPCR	Optional	√
	Residual protein	NanoOrange assay	Optional	√
	Residual solvents	Gas chromatography	Optional	Optional
	Circularization efficiency (for circRNA)	Denaturing agarose gel electrophoresis	√	Optional
		Capillary gel electrophoresis (CGE)	Optional	√

LNP Encapsulation

VectorBuilder offers lipid nanoparticle (LNP) encapsulation for RNA and plasmid delivery. Our service excels in producing homogeneous LNPs with a high encapsulation efficiency. Additionally, we can help our customers enhance their drug delivery efficiency and target tissues by conjugating tissue-targeting antibodies to LNPs or optimizing the LNP formulations.

Highlights

- Standard (e.g. SM102, ALC-0315, MC3) and custom formulations available
- Can encapsulate various types of RNA/DNA molecules, including mRNA, saRNA, siRNA, Cas9 mRNA/sgRNA mix, circRNA, pDNA, etc.
- High encapsulation efficiency (up to 100%)
- Low (<0.1) polydispersity index (PDI)
- Antibody-conjugated LNPs available

Quality Control (QC)

Table 1. Quality control services for LNP encapsulation.

Attribute	QC assay	Research-grade	GMP-like
Appearance	Visual inspection	√	√
Concentration	RiboGreen assay	√	√
Encapsulation efficiency	RiboGreen assay	√	√
Particle size	Dynamic light scattering (Zetasizer)	√	√
Polydispersity index (PDI)	Dynamic light scattering (Zetasizer)	√	√
Surface charge (Zeta potential)	Dynamic light scattering (Zetasizer)	√	√
Encapsulated RNA integrity	Capillary gel electrophoresis (CGE)	Optional	√
Endotoxin	Kinetic chromogenic assay (KCA)	Optional	√
pH	pH paper	Optional	√
Sterility	Bioburden test	Optional	√

LNP-mRNA QC data

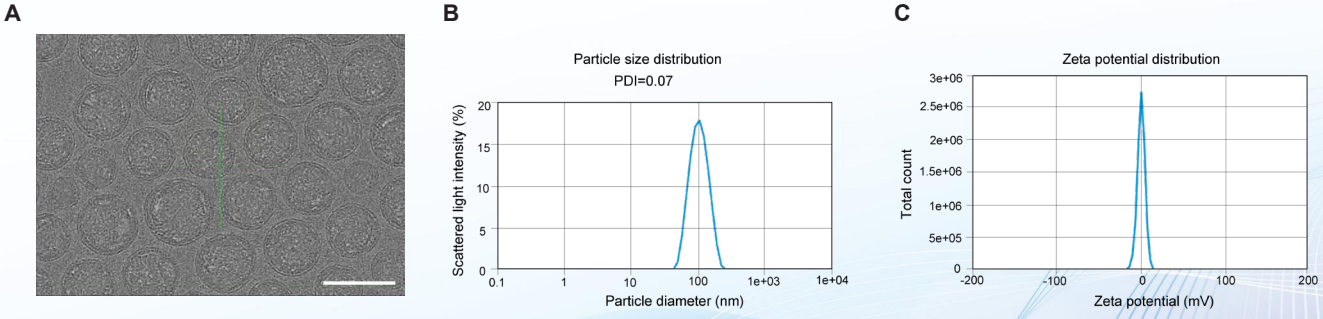


Figure 1. (A) Cryo-TEM micrographs of LNP-mRNA. Scale bar=100 nm. (A) and (B) show particle size and Zeta potential distribution analysis. PDI (B) and Zeta potential (C) were determined by DLS which measures the intensity differences of fluctuated light due to motion of particles. Data demonstrates homogeneous LNP mixtures.

LNP-RNA Functional Validation

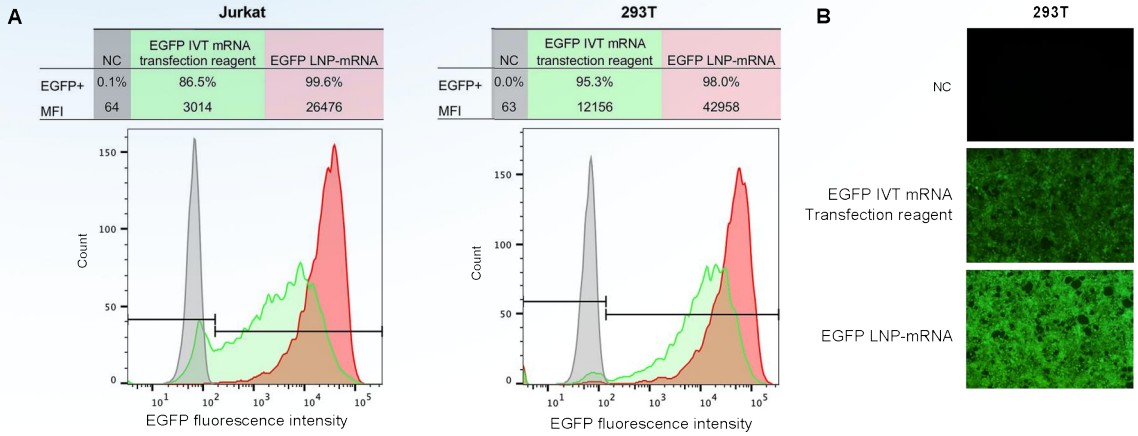


Figure 2. Efficient mRNA delivery and expression using LNP in vitro. Cells were transfected with LNP encapsulated EGFP mRNA or EGFP mRNA mixed with commercial transfection reagent. (A) Flow cytometry analysis of EGFP expression in Jurkat and 293T cells and (B) fluorescent imaging of HEK293T cells at 24 hours post-transfection. MFI: median fluorescence intensity.

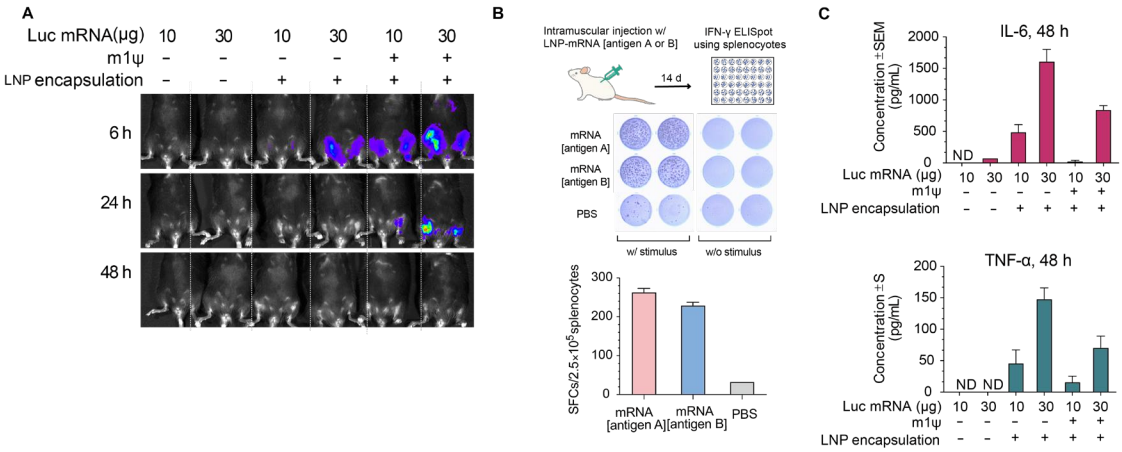


Figure 3. Expression of luciferase (Luc) mRNA and mRNA induced immune response in mice. (A) Luciferase activity visualized by live imaging at 6 h, 24 h, and 48 h post-injection. (B) Two pro-inflammatory cytokines, IL-6 and TNF-α, were quantified in the serum at 48 h post-injection. Error bars represent standard errors. Mice strain: C57BL/6J; mice age: 8 weeks; injection method: intramuscular injection. (C) IFN-γ ELISpot assay of splenocytes derived from Balb/C mice 14 days post intramuscular injection of 30 ug LNP-encapsulated mRNA coding for viral antigen A, viral antigen B, or control PBS.

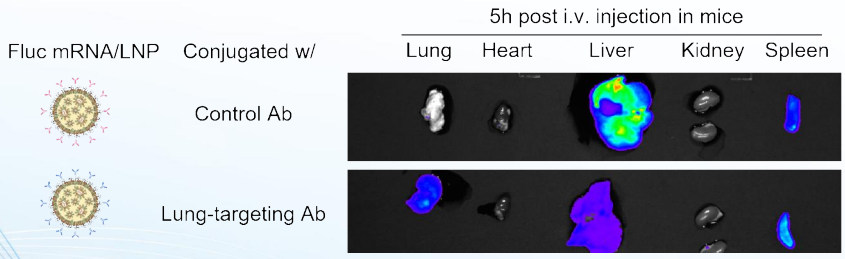


Figure 4. Anti-CD31 conjugated firefly luciferase (FLuc) LNP-mRNA showed improved luciferase expression in lung. Mice strain: C57BL/6J; mice age: 6-8 weeks; mice gender: female; administration route: tail vein. Negative controls: IgG2a-conjugated FLuc LNP-mRNA and naked FLuc mRNA.

IVT mRNA

As a trendy genetic medicine, in vitro transcribed mRNA (IVT mRNA) has several advantages for gene delivery including no risk of insertional mutagenesis, streamlined cell-free manufacturing, and the ability to develop personalized treatments. IVT mRNA can be applied to a wide range of therapeutic applications including vaccines, protein replacement, CAR-T, and CRISPR gene editing. VectorBuilder's expert RNA team specializes in custom IVT mRNA design, production, and LNP encapsulation, with a wide range of customization possibilities.

Highlights

As fast as 5 weeks from vector cloning to LNP encapsulation

Comprehensive customization including capping methods, modified nucleotides, polyA tails, and UTRs

Expert design and production team specialized in optimizing your mRNA for the highest expression, yields, and quality

CRISPR Gene Editing

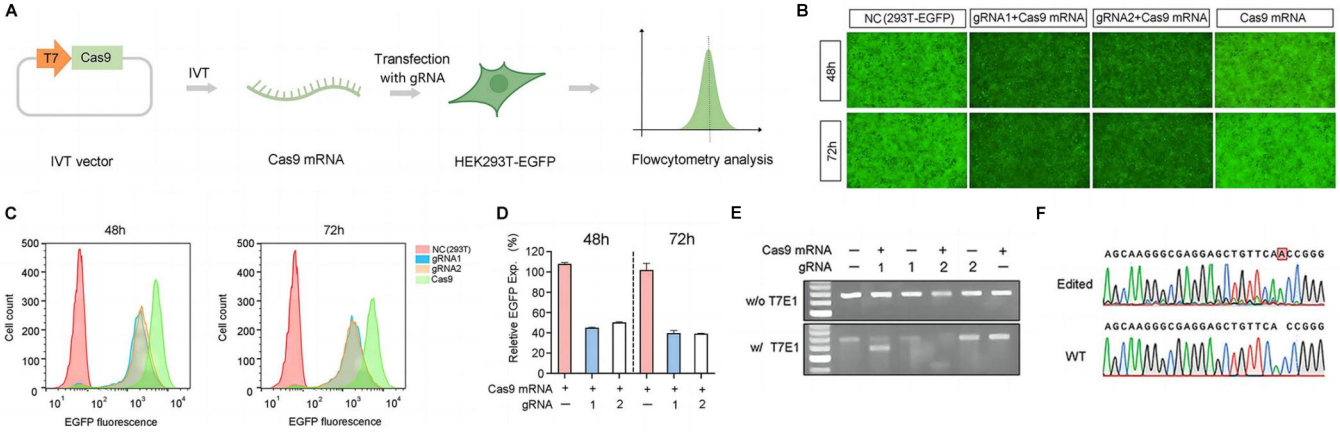


Figure 1. Validation of hSpCas9 mRNA in vitro. (A) IVT Cas9 mRNA was transfected into 293T-EGFP cells with two types of EGFP-targeting gRNA. EGFP expression in non-treated (NC) and transfected cells was observed by microscopy (B) and quantified using flow cytometry (C, D). The editing to EGFP genes on the genome was further confirmed by T7E1 assay and Sanger sequencing (E, F).

CAR-T

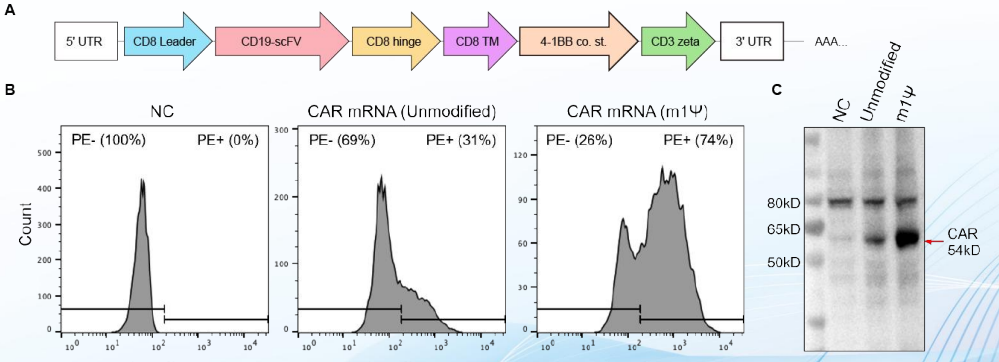


Figure 2. Validation of IVT chimeric antigen receptor (CAR) mRNA expression in 293T cells. (A) CD19 CAR mRNA with robust 5'/3' UTRs and polyA was generated with or without N1-Methylpseudouridine (m1Ψ) and used to transfect 293T cells. (B) 24h post-transfection, cells were incubated with PE-labeled human CD19 to quantify CAR expression using FACS. (C) The expression was further validated using an anti-CD3 zeta antibody and western blot.

VectorBuilder

IVT circRNA

Circular RNA (circRNA) is a covalently closed single-stranded RNA species that does not require capping or a polyA tail and exhibits prolonged transgene expression compared to linear mRNA due to altered degradation kinetics. With these favorable characteristics, IVT circRNA is rapidly being developed for therapeutic applications including vaccines, treating genetic disorders, and modulating the immune system. VectorBuilder specializes in custom circRNA production at a variety of scales.

Highlights

Proprietary sequence optimization for coding region and IRES

Experts design and production team for delivering circRNA with high yield, purity, and expression

Comprehensive QC Panel

Technical Information

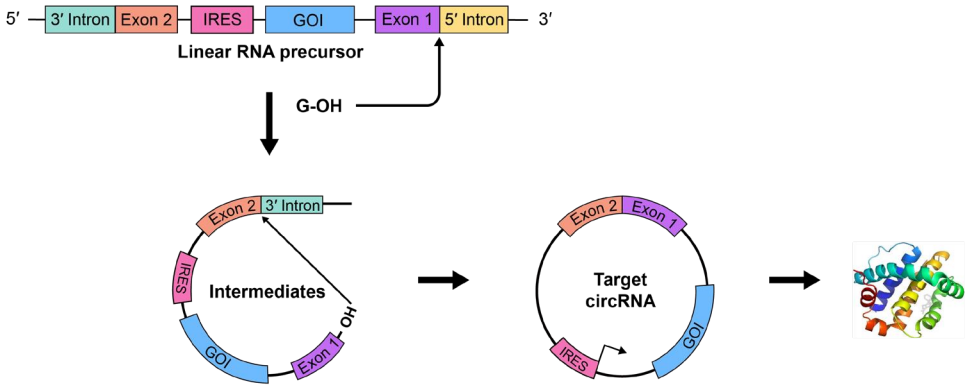


Figure 1. Mechanism of circRNA self-splicing and generation in vitro. The translation of circRNA is IRES dependent.

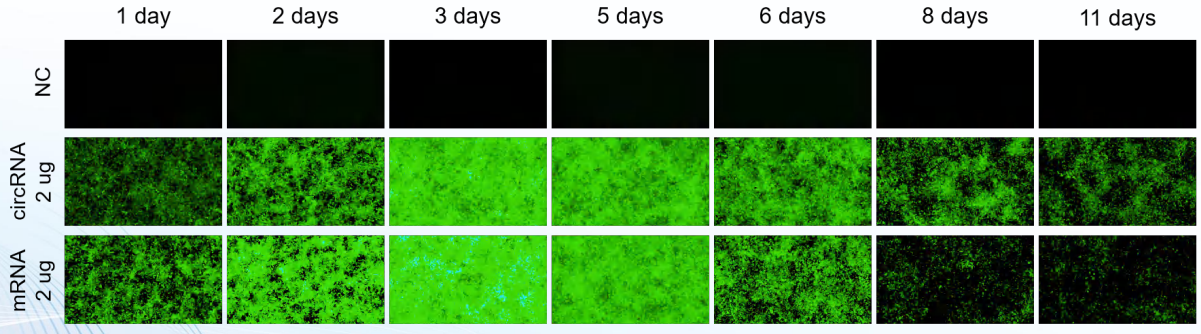


Figure 2. circRNA encoding EGFP was transfected into HEK293T cells and exhibited long-term expression compared to traditional mRNA.

IVT saRNA

Self-amplifying RNA (saRNA) has increased and prolonged expression than traditional mRNA due to its self-amplification capability. Such capability is achieved by incorporating viral sequences (that encode a replicase and replicon elements) in the RNA structure to allow RNA-dependent replication. As the dosing requirements for a robust immune response is far less for saRNA than mRNA, this technology is rapidly being adapted for the next generation of RNA vaccines, and in addition, is a promising candidate for protein replacement. Sequence optimization and the production process for saRNA is similar to mRNA and VectorBuilder specializes in the design and production of high-quality saRNA for a variety of applications.

Highlights

As fast as 5 weeks from vector cloning to LNP encapsulation

Proprietary sequence optimization for optimal expression

Expert design and production team specialized in optimizing your saRNA for the highest expression, yields, and quality

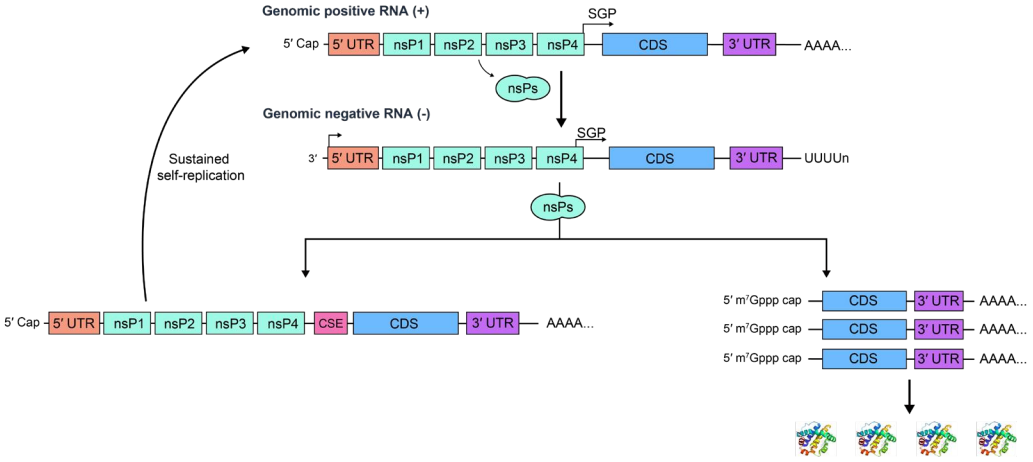


Figure 1. Mechanism of saRNA replication.

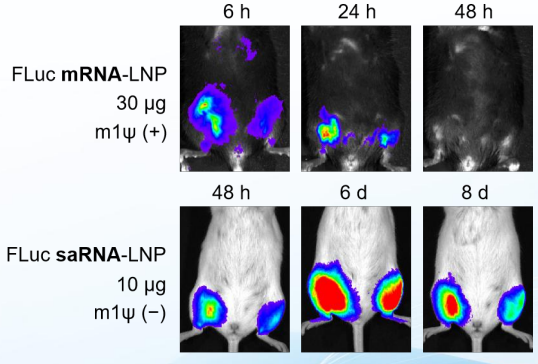


Figure 2. saRNA exhibits prolonged expression compared to standard mRNA in vivo. Expression of 30 ug of LNP-encapsulated firefly luciferase (FLuc) mRNA compared to 10 ug of its saRNA counterpart. Expression of traditional mRNA is no longer observed after 48 hours, whereas saRNA expression persists up to 8 days after intramuscular injection.

Premade IVT RNA and LNP Products

VectorBuilder offers off-the-shelf and ready-to-use IVT RNA and LNP-RNA products for in vitro and in vivo experiments. Their quality and efficacy have been fully validated in both cell culture and animal models, thus, they can be used to assess the efficiency of RNA delivery and expression or used as control for your RNA experiment.

Table 1. RNA products list.

Catagory	Catalog #	Products	Nucleotide	Scale	Price (USD)
mRNA	NR1010-0100	EGFP IVT mRNA	Unmodified	100 ug	$249
	NR1010-1000	EGFP IVT mRNA	Unmodified	1 mg	$1,399
	NR1011-0100	EGFP IVT mRNA	m1Psi	100 ug	$329
	NR1011-1000	EGFP IVT mRNA	m1Psi	1 mg	$1,499
	NR1020-0100	HiExpress™ Firefly Luciferase IVT mRNA	Unmodified	100 ug	$299
	NR1020-1000	HiExpress™ Firefly Luciferase IVT mRNA	Unmodified	1 mg	$1,899
	NR1021-0100	HiExpress™ Firefly Luciferase IVT mRNA	m1Psi	100 ug	$369
	NR1021-1000	HiExpress™ Firefly Luciferase IVT mRNA	m1Psi	1 mg	$2,099
	NR1030-0100	mCherry IVT mRNA	Unmodified	100 ug	$249
	NR1030-1000	mCherry IVT mRNA	Unmodified	1 mg	$1,399
	NR1031-0100	mCherry IVT mRNA	m1Psi	100 ug	$329
	NR1031-1000	mCherry IVT mRNA	m1Psi	1 mg	$1,499
	NR1040-0100	hSpCas9 IVT mRNA	Unmodified	100 ug	$319
	NR1040-1000	hSpCas9 IVT mRNA	Unmodified	1 mg	$1,690
	NR1041-0100	hSpCas9 IVT mRNA	m1Psi	100 ug	$399
	NR1041-1000	hSpCas9 IVT mRNA	m1Psi	1 mg	$2,090
	NR1050-0100	HiExpress™ Guassia Luciferase IVT mRNA	Unmodified	100 ug	$299
	NR1050-1000	HiExpress™ Guassia Luciferase IVT mRNA	Unmodified	1 mg	$1,899
	NR1051-0100	HiExpress™ Guassia Luciferase IVT mRNA	m1Psi	100 ug	$369
	NR1051-1000	HiExpress™ Guassia Luciferase IVT mRNA	m1Psi	1 mg	$2,099
	NR1070-0010	Zebrafish EGFP IVT mRNA	Unmodified	10 ug	$359
	NR1080-0100	HiExpress™ Chicken Ovalbumin IVT mRNA	Unmodified	100 ug	$299
	NR1080-1000	HiExpress™ Chicken Ovalbumin IVT mRNA	Unmodified	1 mg	$1,899
	NR1080-0100	HiExpress™ Chicken Ovalbumin IVT mRNA	m1Psi	100 ug	$369
	NR1080-1000	HiExpress™ Chicken Ovalbumin IVT mRNA	m1Psi	1 mg	$2,099

Table 1. (continued)

Catagory	Catalog #	Products	Nucleotide	Scale	Price (USD)
mRNA	NR1090-0100	Anti-hCD19-h28zCAR IVT mRNA	Unmodified	100ug	$349
	NR1090-1000	Anti-hCD19-h28zCAR IVT mRNA	Unmodified	1 mg	$2,099
	NR1100-0100	Anti-hCD19-hBBzCAR IVT mRNA	Unmodified	100ug	$349
	NR1100-1000	Anti-hCD19-hBBzCAR IVT mRNA	Unmodified	1 mg	$2,099
circRNA	NC1010-0100	IRES-EGFP IVT circRNA	Unmodified	100 ug	$2,799
	NC1010-1000	IRES-EGFP IVT circRNA	Unmodified	1 mg	$16,799
saRNA	NS1010-0100	EGFP IVT saRNA	Unmodified	100 ug	$749
	NS1010-1000	EGFP IVT saRNA	Unmodified	1 mg	$4,099
	NS1011-0100	EGFP IVT saRNA	m5C modified	100 ug	$1,099
	NS1011-1000	EGFP IVT saRNA	m5C modified	1 mg	$6,699
	NS1020-0100	HiExpress™ Firefly Luciferase IVT saRNA	Unmodified	100 ug	$799
	NS1020-1000	HiExpress™ Firefly Luciferase IVT saRNA	Unmodified	1 mg	$4,599
	NS1021-0100	HiExpress™ Firefly Luciferase IVT saRNA	m5C modified	100 ug	$1,199
	NS1021-1000	HiExpress™ Firefly Luciferase IVT saRNA	m5C modified	1 mg	$6,999
LNP-mRNA	NL1010-0100	EGFP LNP-mRNA	Unmodified	100 ug	$1,099
	NL1010-1000	EGFP LNP-mRNA	Unmodified	1 mg	$6,899
	NL1011-0100	EGFP LNP-mRNA	m1Psi	100 ug	$1,199
	NL1011-1000	EGFP LNP-mRNA	m1Psi	1 mg	$6,999
	NL1020-0100	HiExpress™ Firefly Luciferase LNP-mRNA	Unmodified	100 ug	$1,199
	NL1020-1000	HiExpress™ Firefly Luciferase LNP-mRNA	Unmodified	1 mg	$6,999
	NL1021-0100	HiExpress™ Firefly Luciferase LNP-mRNA	m1Psi	100 ug	$1,299
	NL1021-1000	HiExpress™ Firefly Luciferase LNP-mRNA	m1Psi	1 mg	$7,199
	NL1030-0100	HiExpress™ Cre LNP-mRNA	Unmodified	100 ug	$1,199
	NL1030-1000	HiExpress™ Cre LNP-mRNA	Unmodified	1 mg	$6,999
	NL1031-0100	HiExpress™ Cre LNP-mRNA	m1Psi	100 ug	$1,299
	NL1031-1000	HiExpress™ Cre LNP-mRNA	m1Psi	1 mg	$7,199
	NL1040-0100	HiExpress™ FLuc GalNac LNP-mRNA	Unmodified	100 ug	$1,199
	NL1040-1000	HiExpress™ FLuc GalNac LNP-mRNA	Unmodified	1 mg	$6,999
	NL1041-0100	HiExpress™ FLuc GalNac LNP-mRNA	m1Psi	100 ug	$1,299
	NL1041-1000	HiExpress™ FLuc GalNac LNP-mRNA	m1Psi	1 mg	$7,199

RNA CDMO Services

VectorBuilder offers a full range of CRO and CDMO services for in vitro transcription (IVT) mRNA manufacturing and lipid nanoparticle (LNP) therapeutic development. Relying on our revolutionary vector design platform and extensive experience, we can provide optimal in vitro transcription vector designs, large-scale IVT mRNA manufacturing, and LNP encapsulation followed by thorough quality control tailored to a wide range of research and clinical needs. We offer several grades that cover different downstream needs including drug discovery research and pre-clinical studies.

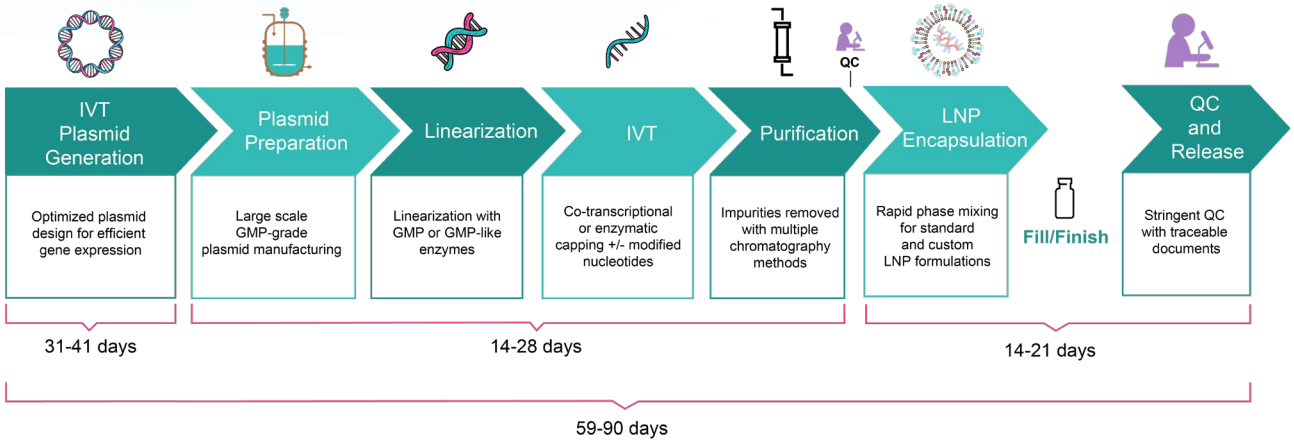


Figure 1. Typical workflow of mRNA CDMO services.

Grades of mRNA Offered

Table 1. Comparison of different grades of IVT mRNA.

	Research-grade	GMP-like
Applications	Basic research, drug discovery, and preclinical studies	Preclinical studies such as animal testing of drug safety and metabolism
Production scales	mRNA: 0.1-10 mg LNP: 0.1-3 mg	mRNA: 0.01-20 g LNP: 3-20 mg
Turnaround time	49-71 days • Vector design & cloning: 26-36 days • Plasmid production & linearization: 14-21 days • IVT mRNA production: 14-21 days • LNP encapsulation: 9-14 days	59-90 days • Vector design & cloning: 31-41 days • Plasmid production & linearization: 14-28 days • IVT mRNA production: 14-28 days • LNP encapsulation: 14-21 days
Quality system	ISO9001	ISO9001 while adopting key features of GMP system
Production facility	In parallel production in shared laboratory space	Productions done in segregated suites
Document control and traceability	No	Yes
QC and release	Standard QC	Performed on a case-by-case basis depending on individual project needs
Aseptic fill/finish	N/A	Available upon request
Storage of retention sample	Available upon request	Available upon request
Other deliverable	COA	1. COA 2. Manufacturing summary 3. TSE/BSE statement upon request

- **Research-grade**

Research-grade mRNA is intended for basic research and drug discovery studies. It is made under standard laboratory conditions with stringent QC to ensure high quality suitable for all downstream research needs.

- **GMP-like**

GMP-like mRNA is intended for pre-clinical studies such as animal testing of drug safety and metabolism. It is produced in a manner that adopts key features of GMP guidelines, including comparable production process and similar quality attributes. Production is performed in segregated production suites with document control and traceability. GMP-like grade can thus be viewed as a small-scale mimic of the final GMP product, but with much lower cost and faster timeline. Where appropriate, GMP-like mRNA can be produced under RNase-free fermentation and purification conditions. A certificate of analysis (COA) is provided at the product release. TSE/BSE statement is available upon request.

- **GMP-grade**

GMP-grade mRNA is produced in our certified GMP suite with strict adherence to GMP guidelines. A comprehensive quality assurance system is implemented throughout the production process. A wide range of in-process and release QC assays are performed to ensure that the mRNA meets or exceeds the desired quality and safety standards. A batch release report fully documenting the production process and a COA are provided at product release. Other documentation is available upon request.

Quality Control (QC) Assays

Standard QC assays include Sanger sequencing, denaturing agarose gel electrophoresis, UV-Vis spectrometry for IVT mRNA and encapsulation efficiency, diameter, PDI and Zeta potential for LNP-mRNA. For individual projects with personalized QC demands, QC assays are performed on a case-by-case basis (see below).

Table 2. Quality control services for IVT DNA template, mRNA, and LNP products.

Product	Attribute	Analytical assay
IVT DNA template	Concentration	Spectrometry
	Identity	Gel electrophoresis, Sanger sequencing
	Linearization	Capillary gel electrophoresis
	Residual host E.coli DNA	qPCR
mRNA	Concentration	UV-Vis spectrometry
	Identity	Capillary gel electrophoresis, reverse transciption followed by Sanger sequencing
	Capping efficiency	LC-MS, Cappillary gel electrophoresis
	PolyA tail integrity	LC-MS, Cappillary gel electrophoresis
	Residual protein	NanoOrange assay
	Residual plasmid	qPCR
	dsRNA	Dot blot
	Endotoxin	Kinetic chromogenic assay (KCA)
LNP	Endotoxin	Kinetic chromogenic assay (KCA)
	Encapsulation efficiency	RiboGreen assay
	Diameter, PDI, and Zeta potential	Zetasizer

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