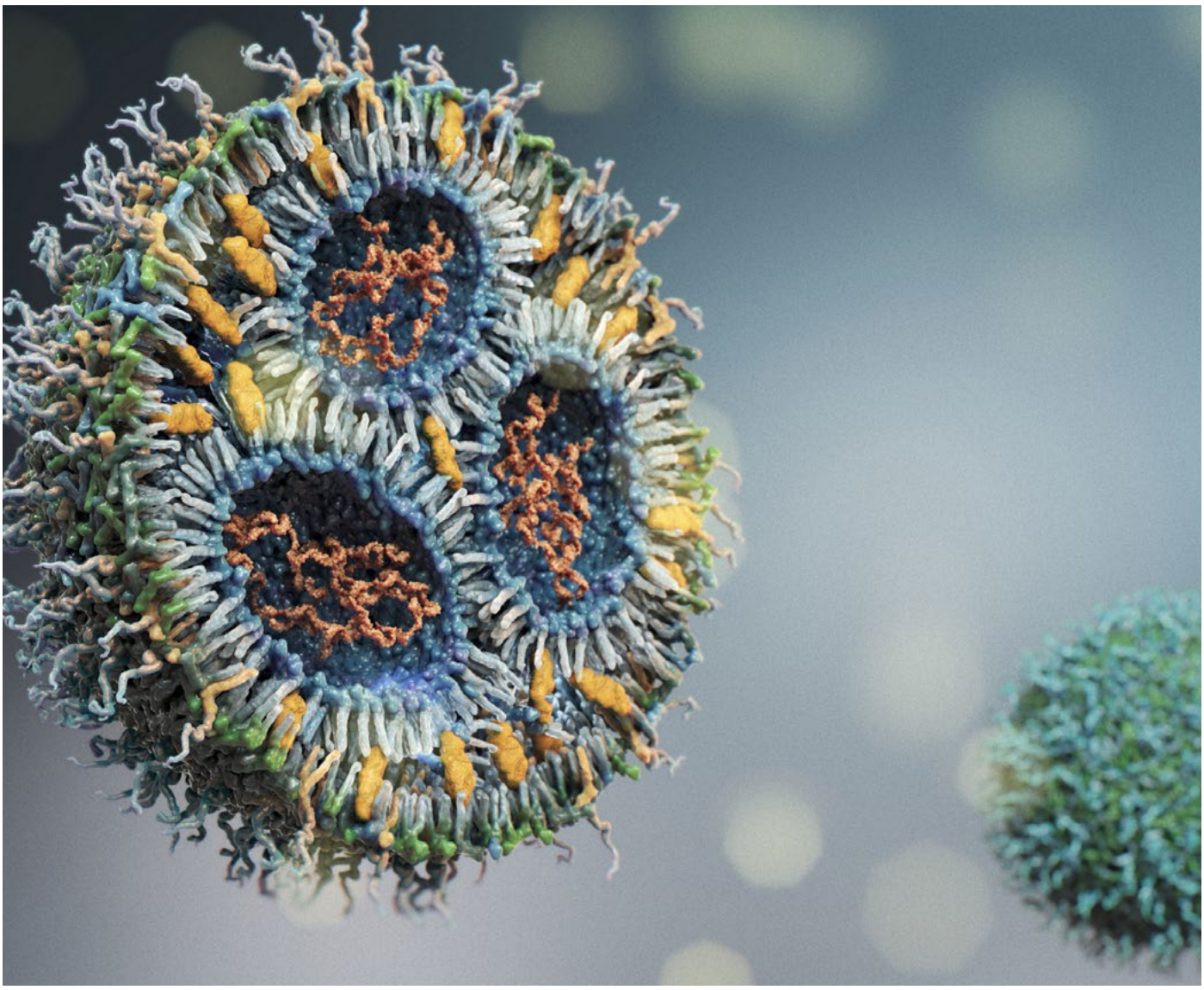
SCIEX

Reach new analytical frontiers in mRNA-LNP



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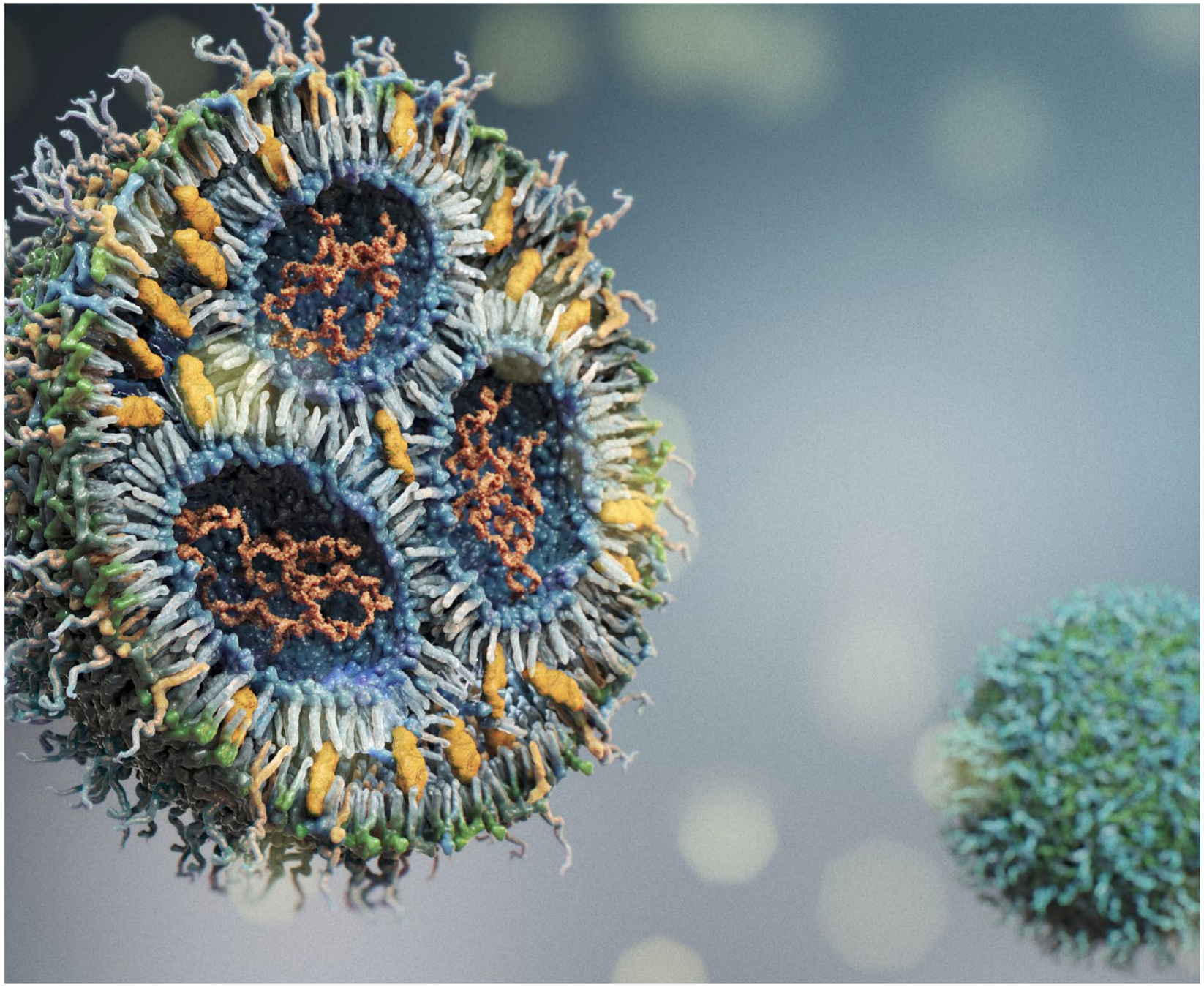
The power of precision

Contents



Introduction

Lipid nanoparticles (LNPs) are widely used to deliver vaccines and therapeutics, such as in vitro transcribed (IVT) RNA, small interfering RNA (siRNA), antisense oligonucleotides (ASOs), and more.

The flexibility of LNPs regarding the type and size of the cargo, limited adverse effects, and easier scale-up compared to viral vectors are factors that contribute to the increased use of LNPs as delivery vehicles.

Understanding product quality and limiting impurities can help mitigate risks to patient safety and ensure product efficacy. As a result, it is essential to characterize critical starting materials, drug substances, and drug products.

Discover how you can break through analytical boundaries with innovative, streamlined technology that provides relevant answers about your LNP-based drugs.

01

Lipid nanoparticles

Lipid nanoparticles

Lipid nanoparticles (LNPs) are widely used for the delivery of vaccines and therapeutics, such as in vitro transcribed (IVT) RNA, small interfering RNA (siRNA), antisense oligonucleotides (ASOs), and more.

Four different classes of lipids are used within LNPs: ionizable cationic lipids or cationic lipids, sterol lipids, helper lipids, and PEG-lipids. The flexibility of LNPs regarding the type and size of the cargo, limited adverse effects and easier scale-up compared to viral vectors are factors that contribute to the increased use of LNPs as delivery vehicles. As a result, it is important to analyze lipid raw material quality, characterize the lipids in the drug products, and perform bioanalysis studies to help mitigate risks to patient safety and drug efficacy.

"LNPs pose unique analytical challenges, in part due to the complexity of their lipid excipients. Consequently, the detailed structure elucidation capabilities afforded by electron-activated dissociation (EAD) in the ZenoTOF 7600 system from SCIEX provide the analytical chemist unparalleled capacity to identify problematic oxidative impurities inside ionizable lipids, and thereby de-risk the LNP therapeutic development process and expedite paths to the clinic."

Adam Crowe (PhD)
Sr. Manager Analytical Development, Cytiva

Raw material and LNP characterization

Explore how to perform comprehensive structural elucidation of lipid raw materials and lipids from LNPs.

MetID and bioanalysis

Overcome matrix complexity to perform identification of metabolites (metID) from lipids and bioanalysis studies.

Lipid quantitation

Streamline the quality control of raw material and the bioanalysis of LNPs with efficient and sensitive analytical technology.

Expert Q&A:

Lipid impurity analysis with LC-MS/MS and EAD

Characterizing the lipid raw material is a crucial step towards the successful development of LNP-based drugs. Dr. Adam Crowe explains why and provides insights into the learnings from his team based on many years of research on a variety of ionizable lipids.

In your opinion, what are the best analytical techniques for assessing the purity of ionizable lipids?

At Cytiva, my team and I use at least three different methodologies to look at quality. We use charged aerosol detection (CAD) for the overall profile, the liquid chromatography coupled to tandem mass spectrometry (LC-MS/MS) with EAD method described in my webinar, and a fluorescence-based assay. The assessment should not be taken lightly, in my opinion. The detailed analysis of the ionizable lipid is paramount for the success of a project. In my experience, one of the most common ways that clinical programs based on LNPs fail is a lack of careful assessment of the raw material.

Can you detect N-oxides with CAD?

Yes and no. You will run into two problems. N-oxides tend to elute very close to the main peak of the ionizable lipid. While you can chromatographically separate them, the gradients required are quite long and you will need prior expertise in what you are trying to separate. The other issue is the relative abundance. Because the N-oxides are an intermediate product that degrades further, you never form huge amounts of it. At ~0.1% relative abundance is when I started to get concerned about N-oxide formation. This makes it difficult for CAD to detect N-oxides because of the method's limited dynamic range, adding to the challenge of having to know what to look for.

At which levels do N-oxides impact mRNA efficacy?

This is an interesting question. It seems in very, very low abundance. We've had the luxury of looking at the adduct formation of 20 to 30 different ionizable lipids. Since the N-oxide itself is not reacting with the mRNA, but presumably an aldehyde—a degradation product of the N-oxide as described by Packer et al. in 2021—predictions are challenging. As a summary, I can say that when N-oxides are present in a significant quantity, meaning ≥1% abundance, we see very significant adduct formation.

Do you have any thoughts on acceptable levels of N-oxides or adducts?

As I mentioned before, N-oxide levels above a 0.1% threshold is where we start to consider adduct formation a problem. However, it is the lipidation event itself that you will need to monitor and do rate calculations on to assess the severity. This is because the N-oxides are diagnostic, but not necessarily predictive of the rate of adduct formation. There are cases where you can see relatively low N-oxide amounts, but the rate of adduct formation on the RNA is quite fast.

In such cases, it is likely that the N-oxides have already degraded to another reactive species.

Do you use MS/MS with EAD only for raw materials, or do you also monitor N-oxides in formulated LNPs?

You can absolutely use the LC-MS/MS with EAD method I presented in my webinar for formulated LNPs. It's obviously less complex to investigate a particular raw material compared to a formulated LNP because you have less species in a sample. However, it can absolutely be done. I recommend reaching out to your SCIEX representative as they might have further information on that topic.

Can you elaborate on how much MS method optimization is typically required and how much time you need to process the data? Can you efficiently transfer methods to new lipids?

It's not a whole lot. Although EAD is very tunable, there are very discrete ranges for the type of fragmentation we are seeking for ionizable lipids. Generally, lipids require high-energy fragmentation for achieving relevant bond breakage—we used around 15 electron volt (eV). If you want to determine the behavior of your specific lipids, you can set up a method with different energies within one injection. The data obtained by EAD are fragment-rich and manual analysis can take some time. However, SCIEX provides Molecule Profiler software as a solution, which can process lipid EAD data and does a lot of the interpretation for you. Historically, we would spend almost a week peering through the data and manually assigning the species that are there. Now, this is done in a ~10-minute computational run through the software followed by a manual check, so it's quite convenient.

Could you give some more detailed information about the MS method setup of the ZenoTOF 7600 system? Did you use targeted, data-dependent or data-independent analysis?

The method used was data-dependent acquisition (DDA)—or information-dependent acquisition (IDA), as some people call it in the industry—for fragmenting the top five candidates, combined with an inclusion list. The inclusion list contained the m/z of expected impurities of the ionizable lipid MC3, such as the addition of oxygen, demethylation, water loss, etc. More information on the method settings can be found in this technical note. Depending on your needs, you can increase the candidate ions and adjust the inclusion list.

Do you have recommendations for how to mitigate adduct formation between the ionizable lipid N-oxide and the RNA?

It really comes down to the quality of your ionizable lipid. Ensuring that the amount of oxygen is minimized and that the ionizable lipid is not heated or exposed to oxidizing agents will help reduce the amount of N-oxides. Ensuring that the purification after synthesis is robust will help as well. Generally speaking, you want to carefully consider your manufacturing synthesis, mechanism, route and purification of your ionizable lipid to mitigate lipidation.

Read Q&A blog

Adam Crowe (PhD)
Sr. Manager Analytical Development, Cytiva

Dr. Adam Crowe manages a multi-discipline team at Cytiva, tasked with developing novel analytical assays related to LNPs and nanomaterials for drug delivery. During his tenure, Adam has garnered broad expertise in analyzing particle payloads, physiochemical characteristics, excipients, and in vitro potency using a variety of analytical methodologies. Notably, he leveraged cutting-edge LC-MS technology for LNP characterization. Additionally, Adam is the technical lead for the American Society for Testing and Materials (ASTM) guide document, outlining best analytical practices for the LNP field.

Characterization of lipids and related impurities

Ionizable lipids are key components of LNPs, complexing the negatively charged cargo and facilitating cellular uptake. Their quality is critical for a stable and efficient product. Even a very low abundance N-oxide impurities can lead to a loss of function. Their structural identification and differentiation from other impurities is an analytical challenge. Furthermore, the saturation of double bonds of the lipids could impact the structure of LNPs and affect the final product.

- Fully understand the structures of your cationic or ionizable lipid components using EAD
- Differentiate between oxidated species and accurately localize double bonds or saturations with EAD
- Avoid missing relevant product excipients by leveraging a linear dynamic range >5 orders of magnitude and signal-to-noise enhancement with the Zeno trap

Stop the guesswork – Determine exact locations of oxygen double bounds, saturations, and more

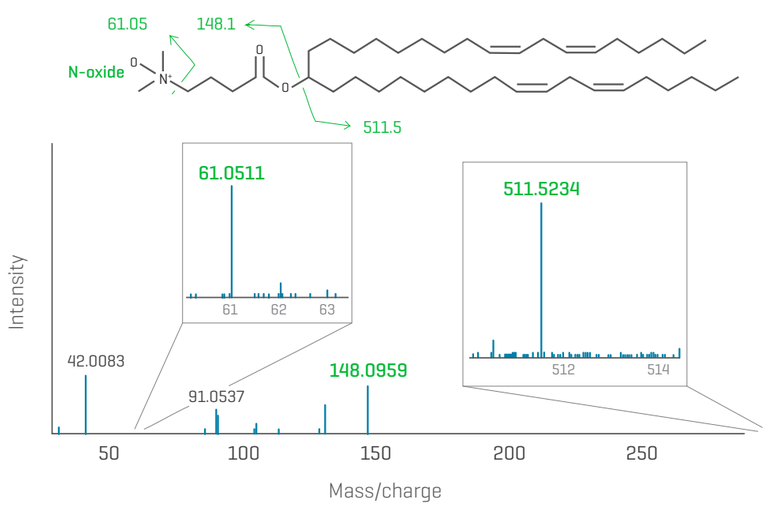
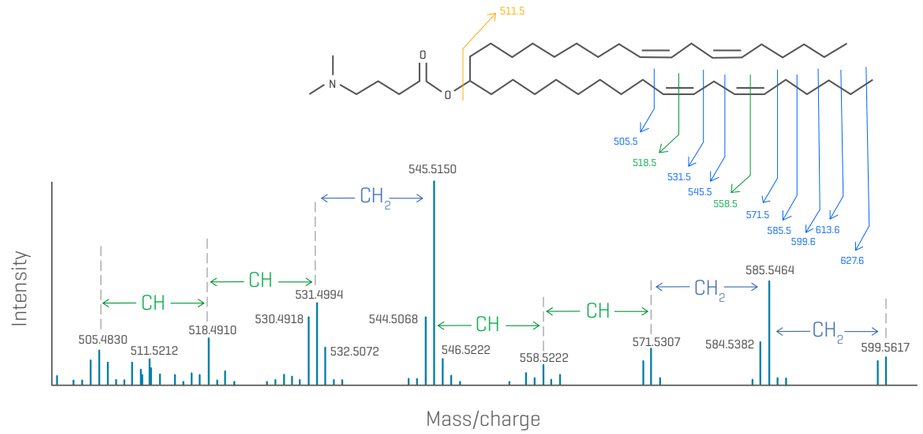


Figure 1: MS/MS EAD data of D-Lin-MC3-DMA (MC3) impurity. EAD-derived fragments can be used to pinpoint oxygen incorporation to the tertiary amine headgroup of MC3. Encircled m/z show diagnostic fragment ions for the identification of an N-oxide impurity derived from MC3.

Figure 2: MS/MS EAD data of MC3. Figure shows a zoom in to the fragmentation data of C-C bonds for structural elucidation and specific localization of double bonds, and saturations with EAD.



Discover more details in the technical notes for MC3 and for ALC-0315

Read technical note **MC3**

Read technical note **ALC-0315**

Streamlined lipid quality control

Commonly, 4 lipid classes (ionizable cationic lipids or cationic lipids, sterol lipids, helper lipids, and polyethylene glycol (PEG) lipids are mixed in defined ratios to form LNPs with desired physical-chemical properties. To ensure quality criteria are met, lipid raw materials and LNP batches need to be monitored. Following lipid characterization and impurity identification, quantitative monitoring can be streamlined.

- Leverage excellent sensitivity for quantitation of lipids and breakdown products in raw materials and formulated LNPs
- Rely on robustness and low %CVs with best-in-class triple quadrupole technology
- Streamline data acquisition and data processing with intuitive software

Detect and quantify different lipid species with high sensitivity and precision

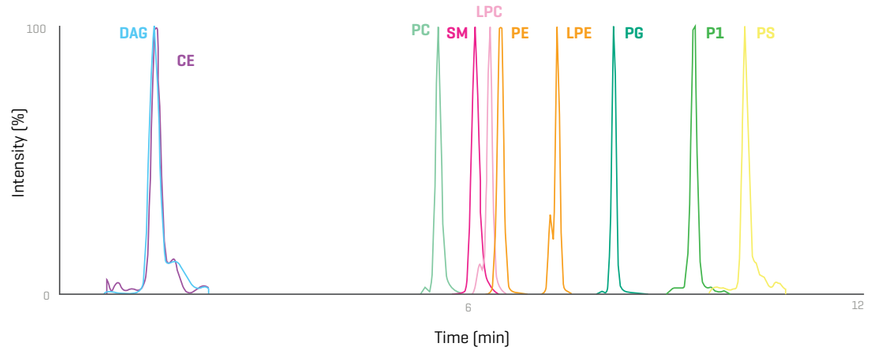


Figure 3: Extracted ion chromatograms for different lipid classes of a liposome with chromatographic separation. Using a normal phase scheduled multiple reaction monitoring (MRM) approach, very good class separation was achieved to avoid isobaric interferences and improve confidence in lipid species identification. Diacylglycerol (DAG), cholesteryl ester (CE), phosphatidylcholine (PC), sphingomyelin (SM), lysophosphatidylcholine (LPC), phosphatidylethanolamine (PE), lysophosphatidylethanolamine (LPE), phosphatidylglycerol (PG), phosphatidylinositol (PI), phosphatidylserine (PS).

Discover more details in the technical note on lipid quantitation from liposomes

Read technical note

Lipid MetID and bioanalysis

Following administration, LNPs can travel to different parts of the body and undergo metabolic changes. Frequently, the non-endogenous cationic or ionizable cationic lipids are used as surrogates for quantitative analyses of LNPs in in vivo samples. Multiple bioanalytical end points from a single administration with small sample volumes require analytical assays with high sensitivity. In addition, matrix interferences and structural elucidation of metabolites need to be overcome.

- Elucidate the structures of your cationic or ionizable lipid components and related metabolites using EAD
- Overcome matrix interferences and achieve outstanding quantitative results for difficult-to-fragment lipids with accurate mass spectrometry and the Zeno trap
- Achieve identification and quantitation of different lipid species and metabolites in parallel

Leverage powerful structural elucidation and quantitation capabilities in one experiment

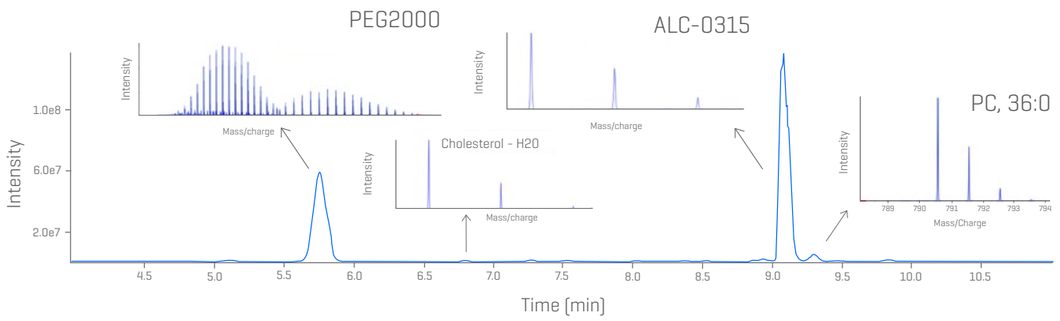
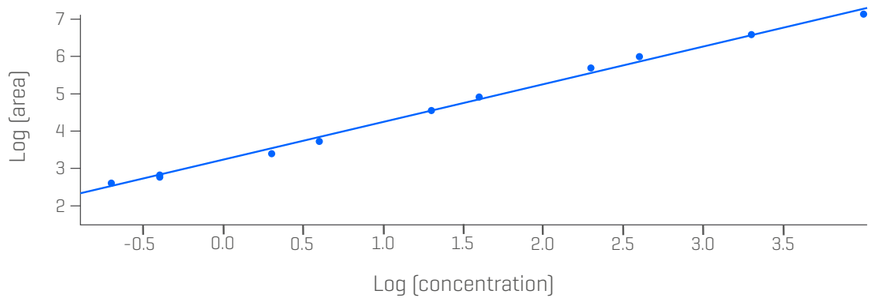


Figure 4: Identification of all four lipid species from an LNP. Total ion chromatogram showing the pegylated lipid 2-[[polyethylene glycol]-2000]-N,N-ditetradecylacetamide, PEG2000, the sterol lipid cholesterol, the ionizable lipid 6-[[2-hexyldecanoyl]oxy]-N-[6-[[2-hexyldecanoyl]oxy]hexyl]-N-[4-hydroxybutyl]hexan-1-aminium (ALC-0315) and PC without unsaturated carbon bonds as helper lipid with related time-of-flight (TOF) MS data.



Row	Component Name	Actual Con...	Num....	Mean	Standard Dev...	Percent CV	Average Accura...	Value #1	Value #2	Value #3
5	ALC-0315 766	0.2000	3 of 3	2.139e-1	3.124e-2	14.61	106.94	2.255e-1	1.785e-1	2.377e-1
6	ALC-0315 766	0.4000	3 of 3	3.467e-1	1.295e-1	37.33	86.69	4.904e-1	3.106e-1	2.392e-1
7	ALC-0315 766	2.0000	3 of 3	1.910e0	2.902e-1	15.19	95.50	1.800e0	2.239e0	1.691e0
8	ALC-0315 766	4.0000	3 of 3	4.084e0	3.449e-1	8.44	102.10	4.451e0	4.035e0	3.766e0
9	ALC-0315 766	20.0000	3 of 3	2.258e1	7.906e-1	3.50	112.90	2.210e1	2.349e1	2.215e1
10	ALC-0315 766	40.0000	3 of 3	3.550e1	9.135e-1	2.57	88.74	3.475e1	3.522e1	3.652e1
11	ALC-0315 766	200.0000	3 of 3	1.739e2	7.365e0	4.23	86.95	1.822e2	1.681e2	1.714e2
12	ALC-0315 766	400.0000	3 of 3	4.255e2	2.031e1	4.77	106.38	4.469e2	4.232e2	4.065e2
13	ALC-0315 766	2000.0000	3 of 3	2.257e3	3.894e1	1.73	112.85	2.275e3	2.284e3	2.212e3
14	ALC-0315 766	10000.0000	3 of 3	1.010e4	9.605e1	0.95	100.95	9.990e3	1.012e4	1.018e4

Figure 5: Calibration curve for ALC-0315. LNPs were spiked into plasma and extracted using solid phase extraction. Calibration curve is based on extracted ion chromatograms run in triplicates.

More questions?

Contact us

Analytical solutions for lipids and LNPs

Suitable for:

- In-depth structural elucidation
- Simultaneous relative quantitation
- High flexibility to perform a range of additional workflows

ExionLC AE system

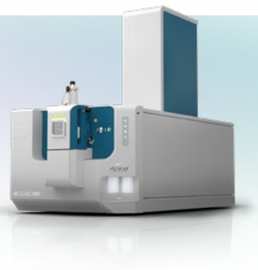
An LC system that seamlessly integrates with your SCIEX MS for reproducible data, batch after batch.

Learn more

ZenoTOF 7600 system

A high-resolution solution, combining powerful MS/MS sensitivity and alternative fragmentation technology.

Learn more



Molecule Profiler software

A software solution to identify impurities and biotransformations for a wide variety of modalities.

Learn more

SCIEX OS software

The next generation of operating and processing solution for an enhanced LC-MS/MS analysis experience.

Learn more

Suitable for:

- Targeted analysis and monitoring
- Excellent quantitative performance

ExionLC AE system

An LC system that seamlessly integrates with your SCIEX MS for reproducible data, batch after batch.

Learn more

SCIEX 7500+ system

A new standard for resilience and robustness, engineered to maintain sensitivity for longer.

Learn more

SCIEX OS software

The next generation of operating and processing solution for an enhanced LC-MS/MS analysis experience.

Learn more

Tips and tricks from our application experts:

Lipid impurity analysis with EAD

Paul Norris (PhD), Sr. Application Support, US at SCIEX, shares his tips and tricks on lipid analysis using LC-MS/MS with EAD.

Tip 1: Establish ideal sample concentrations

Start with a concentration of 20-200 ng/mL in 15:85 (v:v) water:acetonitrile for the ionizable lipid as raw material or as part of a nanoparticle formulation. I recommend targeting a TOF MS signal of >1E5 counts per second (cps) for the extracted ion chromatogram of the ionizable lipid on a ZenoTOF 7600 system and adjusting the concentration accordingly. This will result in high quality EAD spectra. For identification of impurities, I suggest preparing a 100x higher concentration. Since impurities are typically present in much lower abundance, a higher concentration is required to produce ideal EAD spectra. Typically, 2 µg/mL works well, however, concentration may need to be adjusted depending on the signal observed.

Tip 2: Resolve ionizable lipids and impurities

Chromatographic separation of ionizable lipids, their impurities and degradation products works particularly well with reversed phase C18 columns with a larger pore size (e.g., 300 Å). Start with a mobile phase consisting of 15% water and 85% (v:v) organic solvents like acetonitrile or methanol (or a mixture of both) with 10 mM ammonium acetate and a 10 min gradient ending in 100% organic solvent. This should resolve most ionizable lipid impurities and enable clean EAD spectra for characterization. Make sure to include a 5–10-minute wash at 100% organic before re-equilibrating the column.

Tip 3: Attain comprehensive ionizable lipid fragmentation

Comprehensive EAD spectra can be obtained by using optimized parameters based on the lipid structure. From my experience, an electron beam current at 5000 nA and an electron kinetic energy from 12—16 eV work best for most ionizable lipids. These settings also work well for most natural structural lipids with a similar size and structural composition (e.g., phosphatidylcholines). Great spectral quality with high signal-to-noise can be achieved with a reaction time of 30—35 ms and an accumulation time of approximately 100 ms.

Tip 4: Set up method for impurities

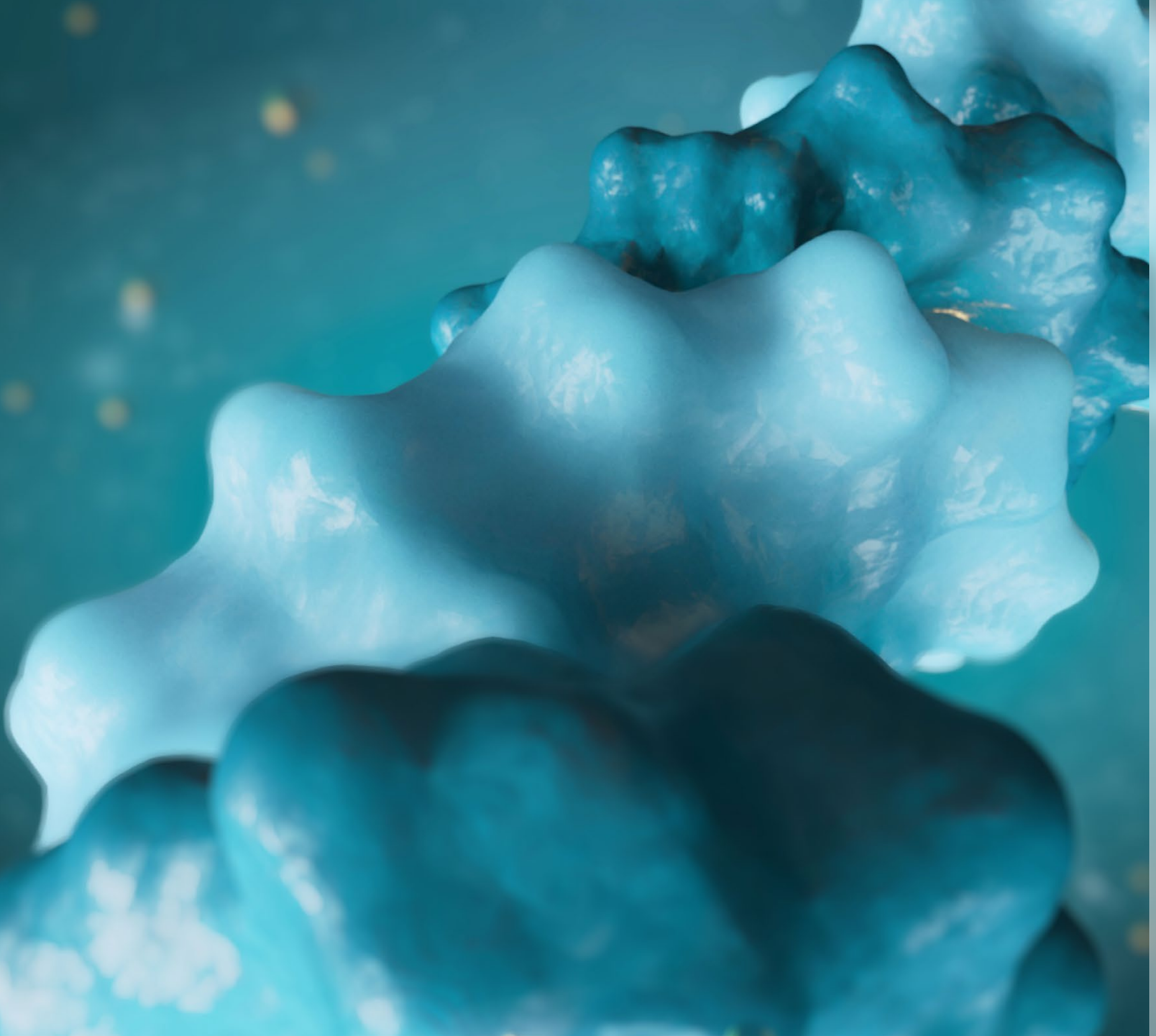
Typical impurities observed for a range of ionizable lipids include N-oxides, epoxides and hydroxyl functional groups at desaturated carbons relative to the parent structure. Additionally, saturation, desaturation, methylation and demethylation of the parent structure can be observed. I recommend designing MS/MS methods that incorporate these putative impurities in an inclusion list within a data-dependent experiment. With that setup, you can achieve detailed MS/MS information of expected impurities and of unknown impurities in your sample.

More questions?

Contact us

Paul Norris (PhD)
Sr. Application Support, US at SCIEX

Paul Norris specializes in the profiling and characterization of bioactive lipid mediators in the context of physiological and pathophysiological processes. He has a wealth of experience maximizing the capabilities of triple quadrupole and Q-TOF solutions for omics discovery and life sciences. Paul's extensive lipidomics experience started in the lab of Edward Dennis at UCSD where he contributed to studies as part of the LIPID MAPS consortium before joining Brigham and Women's Hospital to lead a lipidomics core facility, supporting numerous resolution pharmacology projects.



02

Plasmid DNA

Plasmid DNA

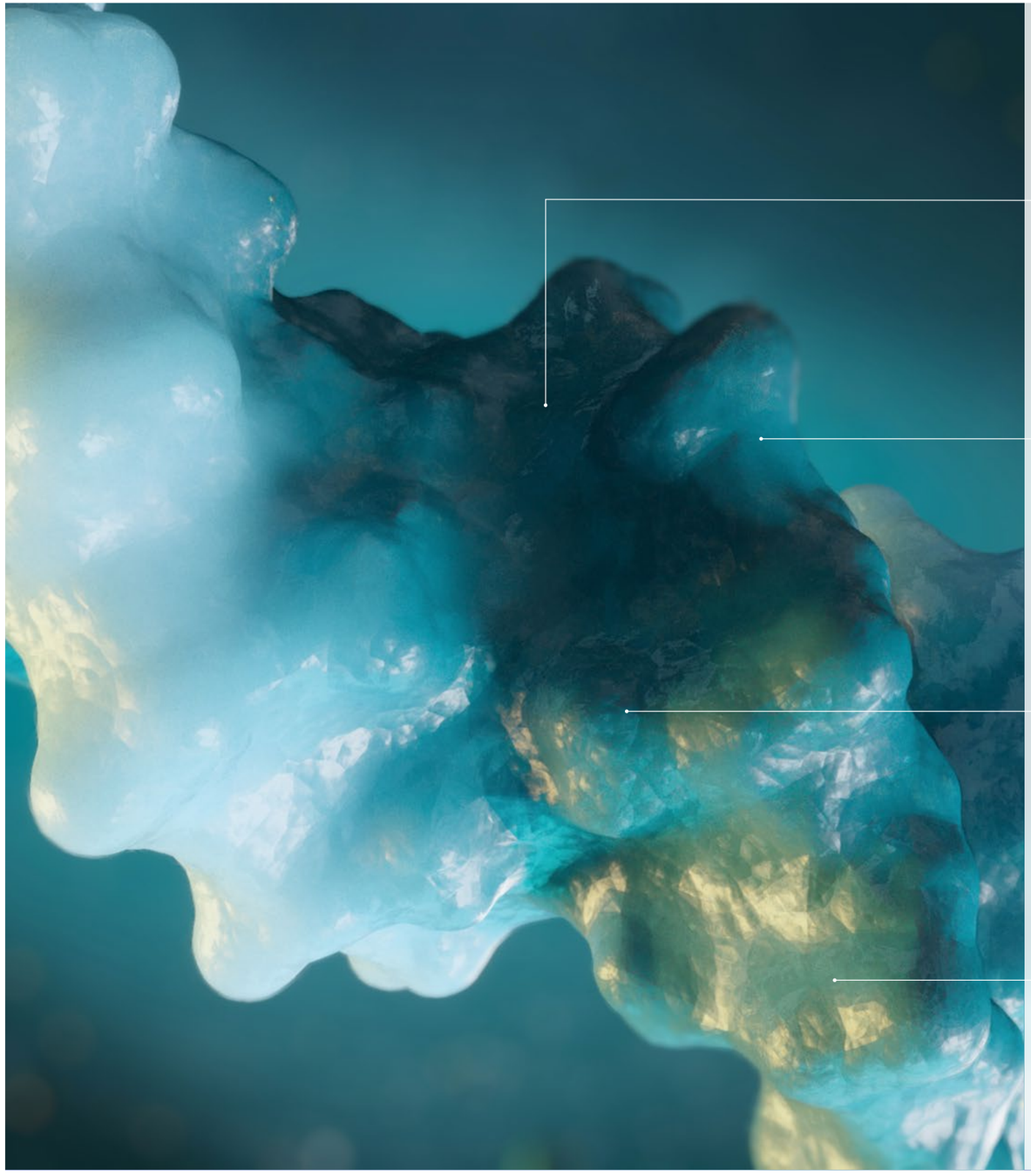
Double-stranded DNA plasmids are an extremely versatile tool frequently used for genetic engineering in biotechnology applications.

In a medical context, plasmid DNA (pDNA) can be used directly—as a vaccine or for ex vivo cell therapy for instance—but also serve as raw or critical starting material for the manufacturing of protein drugs, viral vectors, and mRNA.

Generally, pDNA contains several regions to enable its function within drug manufacturing: An origin for the replication in bacteria, the gene of interest (GOI), a promoter to enable the expression of the GOI, antibiotic resistance genes for selection as needed, and in case of viral vector production, long terminal repeats (LTRs). The pDNA quality directly impacts the quality of subsequent protein, nucleic acid, or viral vector products and must therefore be ensured.

"Plasmid DNA (pDNA) is a widely used starting material in the manufacturing process of mRNA-based vaccines or viral vectors. Consequently, a high pDNA quality must be ensured. Capillary gel electrophoresis with laser-induced fluorescence (CGE-LIF) on a PA 800 Plus system from SCIEX offers accurate and highly sensitive pDNA analyses, enabling a reliable assessment of pDNA quality prior to further processing."

Roman Herzog (PhD)
Group Leader Bioanalytics (R&D), WACKER Chemie AG



pDNA restriction fragments

Achieve excellent resolution over a large size range for fragment-based ID of dsDNA.

Residual nucleic acids

Understand the sizes and amounts of residual host cell nucleic acids.

pDNA purity

Separate plasmid isoforms with high resolution and assess the purity and stability of your pDNA.

Linear DNA size

Determine accurately the size of your linearized pDNAs over a wide size range.

Expert Q&A:

Plasmid manufacturing

Plasmid DNA serves a variety of purposes—from critical starting material for proteins, mRNA or viral vectors to drug substances. Here, Dr. Emma Bjorgum, an expert in plasmid manufacturing provides insights into the process and an outlook on the future.

Learn how to set up your program for success with Aldevron

Learn more

What applications does Aldevron manufacture plasmid DNA for?

Aldevron manufactures plasmid DNA for a variety of end applications. Much of our experience and expertise is comprised of manufacturing plasmid DNA for cell and gene therapy applications. We also manufacture for all phases and stages of pipeline development from early discovery to commercial applications. Aldevron is among the first to offer plasmid DNA at full current Good Manufacturing Practice (cGMP) or clinical grade and has pioneered a mid-grade between research grade and full cGMP, called GMP-Source. This has allowed us to support an estimated 1500 clinical trials run by over 1000 clients. We thrive on supporting clients from the early stages of their clinical programs through commercialization.

How does your support vary by application?

We can provide plasmid DNA for various applications. Two specific examples include support of mRNA and AAV gene therapies and vaccines. For mRNA applications, we provide plasmid DNA as a linearized product and can perform the linearization with a client-designated enzyme. We also screen the plasmid construct prior to manufacturing to optimize conditions for both yield and stability of the poly(A) tail (if encoded). For AAV drugs, we optimize conditions for scale up by evaluating different host cell lines and temperature combinations for inverted terminal repeat (ITR) retention. A third example is our investment in next-generation plasmid technology, Nanoplasmid vectors. Nanoplasmids are comprised of very small, efficient backbones (~500 bases). Removal of bacterial and antibiotic resistance genes improves both safety and performance. One area where Nanoplasmids are showing particularly strong performance is as a homology-directed repair (HDR) donor template for CRISPR knock-in applications.

How do you ensure the quality of your plasmids at the different quality levels you offer?

Aldevron offers a comprehensive quality control testing panel of assays for the release of plasmid DNA. Assays include various methods for identity, safety, bacterial host components, and bioburden/sterility. Almost all our assays are conducted in-house, and methodologies are closely aligned for testing and release of RUO, GMP-Source and GMP methods.

How have the requirements for plasmids changed over the past 5-10 years?

In the earlier days of cell and gene therapy, there were hardly any references to plasmid manufacturing recommendations where plasmid DNA is utilized as a critical starting material or raw material. As cell and gene therapy has continued to see additional approvals, we have seen more recent considerations from the agency for CAR-T therapies with a recommendation to remove any unnecessary transgene in the vector such as antibiotic resistance markers. Aldevron's Nanoplasmid technology ameliorates this concern as it utilizes a sucrose selection technology negating the need for any antibiotics in the manufacturing process.

What changes do you anticipate moving forward?

Moving forward, we are likely to see additional scrutiny on vector backbones and the removal of any extraneous sequences. We are also likely to see increased specificity on scale and how manufacturers can deliver exactly what is needed at the point in time of clinical development. Aldevron is focused on providing the 'right sized' scale for manufacturing and can meet both exact quantity and batch deliverables.

What innovation is helping to drive the industry forward and how will analytics need to evolve?

Newer vector technologies, such as nanoplasmid, can help address concerns with extraneous sequences in the plasmid backbone size since it consists of only 200 bp. Another innovation area is next-generation microbial cell lines to improve the yield and stability of plasmid DNA, such as the REVIVER cell line. Additionally, non-viral delivery systems are tackling challenges in the industry for payload delivery by lowering costs and delivering products without the constraints of a viral system. Additionally, innovation around the client experience is a key focus for us. Over the past 2 years we have been intensely focused on the client experience and have made incredible progress streamlining the new program on-boarding process, reducing lead times, and eliminating deviations. For example, in 2023, we were able to reduce our lead time by up to 80% from construct selection through product release.

mRNA is driving industry growth. How does Aldevron support the mRNA modality from a plasmid perspective?

Aldevron can provide linear plasmid DNA at any scale and quality level (RUO, GMP-Source, and GMP). Our processes allow for linearization with the client-selected enzyme, including a purification step post-linearization to ensure the product is free from any remaining enzyme. We can provide analytical testing for the final linearized product to confirm the percentage of linearized plasmid in addition to poly(A) tail length. Several of our clients get linear plasmid DNA from us and do the IVT and other reactions internally. Increasingly, clients are taking advantage of Aldevron's broader RNA services, including linear plasmid, IVT and capping reactions, lipid nanoparticle encapsulation and sterile fill-finish services. That includes all the associated analytics, such as CGE, for instance.

What additional services are popular with those manufacturing plasmid for clinical applications?

Additional services often required to support plasmid DNA for clinical services include stability testing of both final plasmid DNA products, and master cell banks. Commercialization support services such as process characterization and process validation are also often required in the late phases of clinical development. Additionally, regulatory services are often utilized to support Chemistry, Manufacturing, and Control (CMC) sections of Investigational New Drug (IND) filings or Biologics License Applications (BLAs).

Emma Bjorgum is the Vice President of Client Services of the DNA Business Unit at Aldevron with a focus on product strategy and portfolio management. She has been employed in the cell and gene therapy industry for over a decade with 9 years of experience at Aldevron. Before Aldevron, Emma worked for Millipore Sigma as a Business Development Manager for the Viral and Gene Therapy Manufacturing business unit. She also worked for Be The Match Biotherapies as a Business and Market Analyst. Emma obtained her BA in Biology with minors in Chemistry and Psychology from Concordia College in Moorhead, MN.

pDNA topology and purity

Plasmids can exist in three primary topological forms: covalently closed circular (ccc), often referred to as supercoiled (sc), open-circular (oc), and linear. The sc form is desirable during plasmid manufacturing and for subsequent protein expression, viral vector manufacturing, or DNA vaccines. Differentiating conformational isoforms and assessing the purity and stability of pDNA is crucial for ensuring product quality, whether it is the critical starting material or drug substance.

- Rely on excellent resolution for different topological variants of pDNA
- Achieve high sensitivity for early-stage development samples with LIF detection
- Confidently transfer assays from development to QC with excellent precision and streamline data management through compatibility with data management systems

Differentiate different topological variants and determine purity with ease

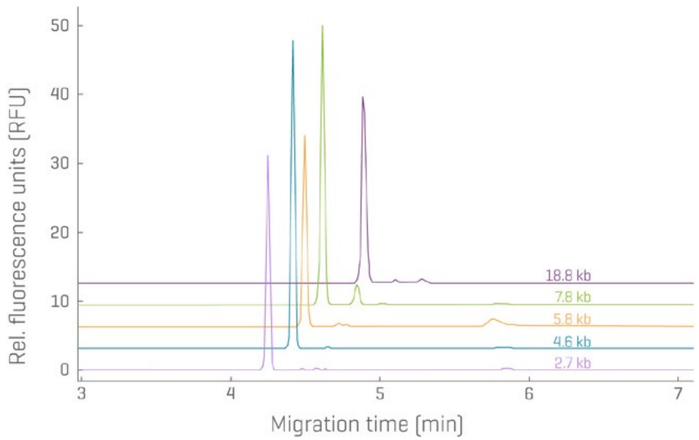


Figure 23: Separation of topological isoforms of 5 plasmids (2.7–18.9 kb) using the DNA 20 kb Plasmid and Linear kit.

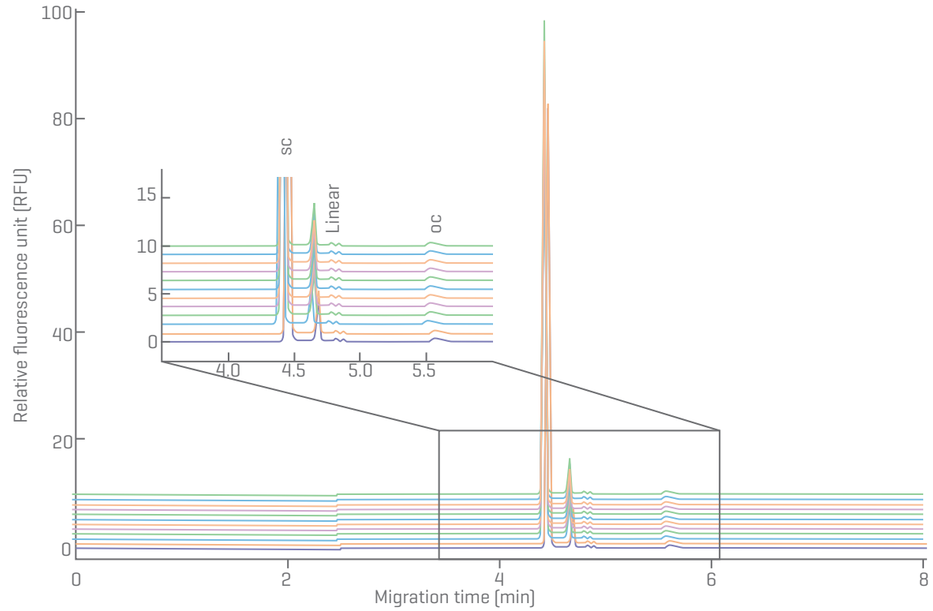


Figure 24: Assay repeatability of a 7.9 kb plasmid. The sample was injected from the same well for 12 consecutive injections and analyzed on the BioPhase 8800 system with a BioPhase BFS capillary cartridge - 8 x 30 cm using the DNA 20 kb Plasmid and Linear kit.

Discover more details in the technical note about plasmid purity monitoring

Read technical note

pDNA linearization efficiency and sizing

Linearized DNA serves as a template for mRNA and other IVT RNAs, and minimizes off-target or elongated mRNA transcripts due to read-through transcription. The linearization efficiency of pDNA is, therefore, an important quality attribute of DNA starting material. Furthermore, sizing of the linearized plasmid and assessment of its purity can help determine the quality of linearized pDNA.

- Determine linearization efficiency with excellent separation for different topological variants of pDNA
- Assess linear DNA sizes and purity confidently with ultra-high resolution over a wide size range
- Confidently transfer assays from development to QC and streamline data management through compatibility with data management systems

Assess linear DNA sizes and purity confidently with ultra-high resolution over a wide size range

Understand linearization efficiency and linear DNA sizes

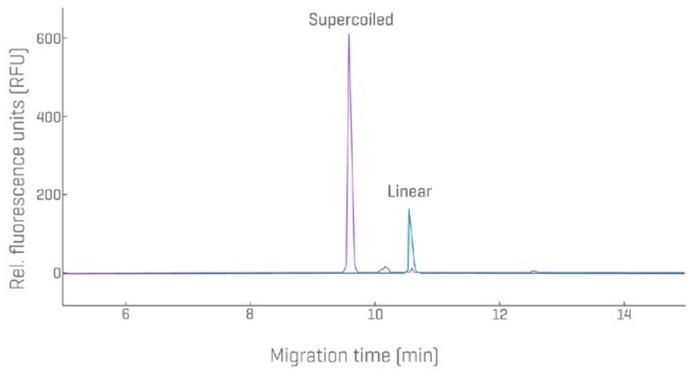


Figure 25: Linearized plasmid purity analysis and size estimation of a 7.9 kb plasmid sample. The electropherogram shows the sample prior to linearization, containing mainly the supercoiled isoform and after linearization.

Baseline separation between 7000 and 8000 bp

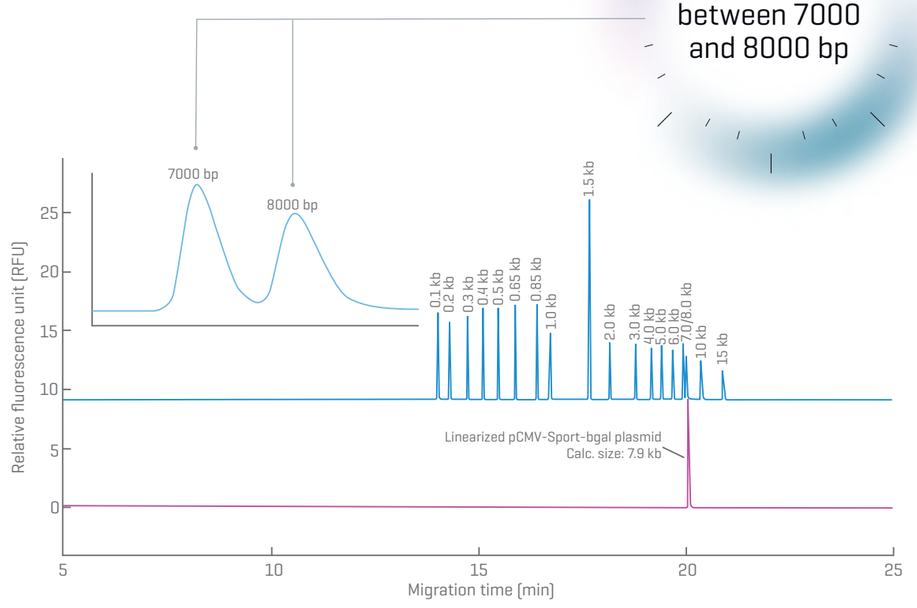


Figure 26: Size determination of the linearized 7.9 kb with a BioPhase BFS capillary cartridge - 8 x 50 cm. Top: The 1 kb Plus DNA Ladder with the inset showing the resolution between the 7,000 bp and 8,000 bp fragments. Bottom: The linearized plasmid sample with calculated size.

Discover more details in the technical note about plasmid purity and linear DNA sizing

Read technical note

pDNA restriction map

Several analytical techniques for plasmid identity testing exist. However, homologous regions, such as poly[A] tails, LTR, and ITR, present a challenge for sequencing-based methods. The repetitive nature of these regions makes it difficult to obtain accurate information on their length and composition. Tailored restriction fragment analysis with high resolving CGE provides an alternative that is not affected by long, homologous pDNA regions.

- Achieve identity testing with excellent resolution of DNA restriction fragments over a wide size range
- Rely on results with excellent accuracy and precision
- Confidently transfer assays from development to QC and streamline data management through compatibility with data management systems

Determine pDNA fragment sizes across a wide range

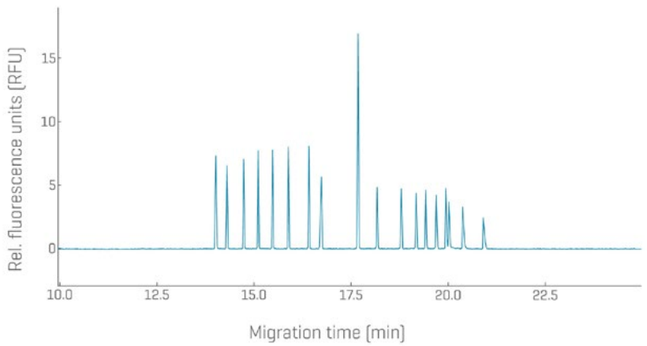


Figure 27: Electropherogram showing baseline separation of a linear dsDNA ladder from 100-15,000 bp.

More questions?

Contact us

Analytical solutions for plasmid DNA

Suitable for:

- pDNA purity analysis
- Linear DNA sizing and fragment analysis
- Larger sample sets

BioPhase 8800 system

Purpose-built for achieving high quality data efficiently across various analytical assays.

Learn more

DNA 20 kb Plasmid and Linear kit

A kit to perform reproducible pDNA purity assessment and size estimation of linear dsDNA with ease.

Learn more

BFS capillary cartridge

A pre-assembled bare-fused silica 8-capillary cartridge available in 30 and 50 cm total length.

Suitable for:

- pDNA purity analysis
- Linear DNA sizing and fragment assessment

PA 800 Plus system

A solution enabling confident decision making and QC-readiness for your biopharmaceutical products.

Learn more

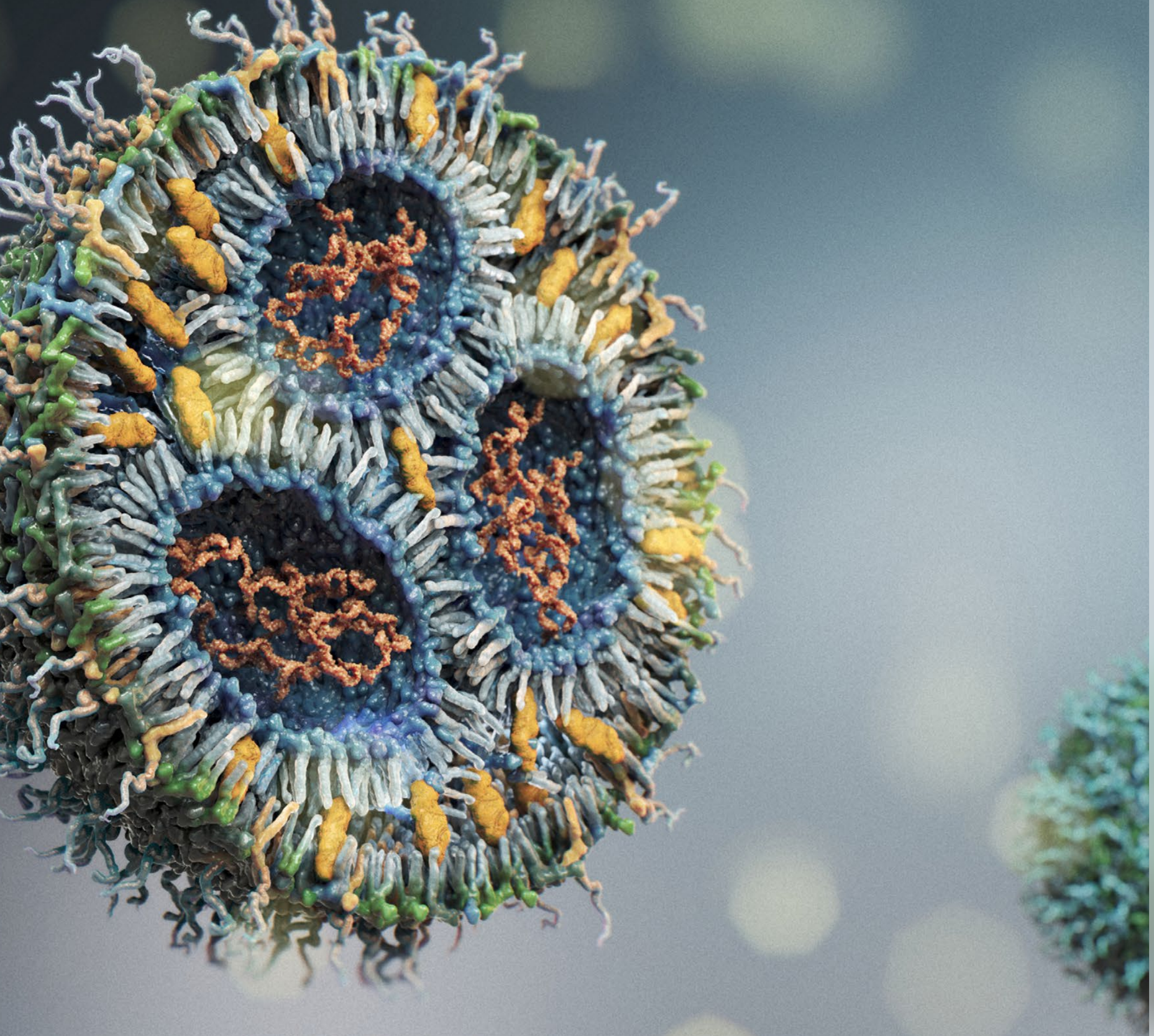
DNA 20 kb Plasmid and Linear kit

A kit to perform reproducible pDNA purity assessment and size estimation of linear dsDNA with ease.

Learn more

BFS capillary cartridge for the PA 800 Plus system

A pre-assembled bare-fused silica single capillary cartridge available in 30 cm total length.



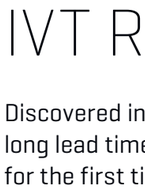
03

IVT RNA

IVT RNA

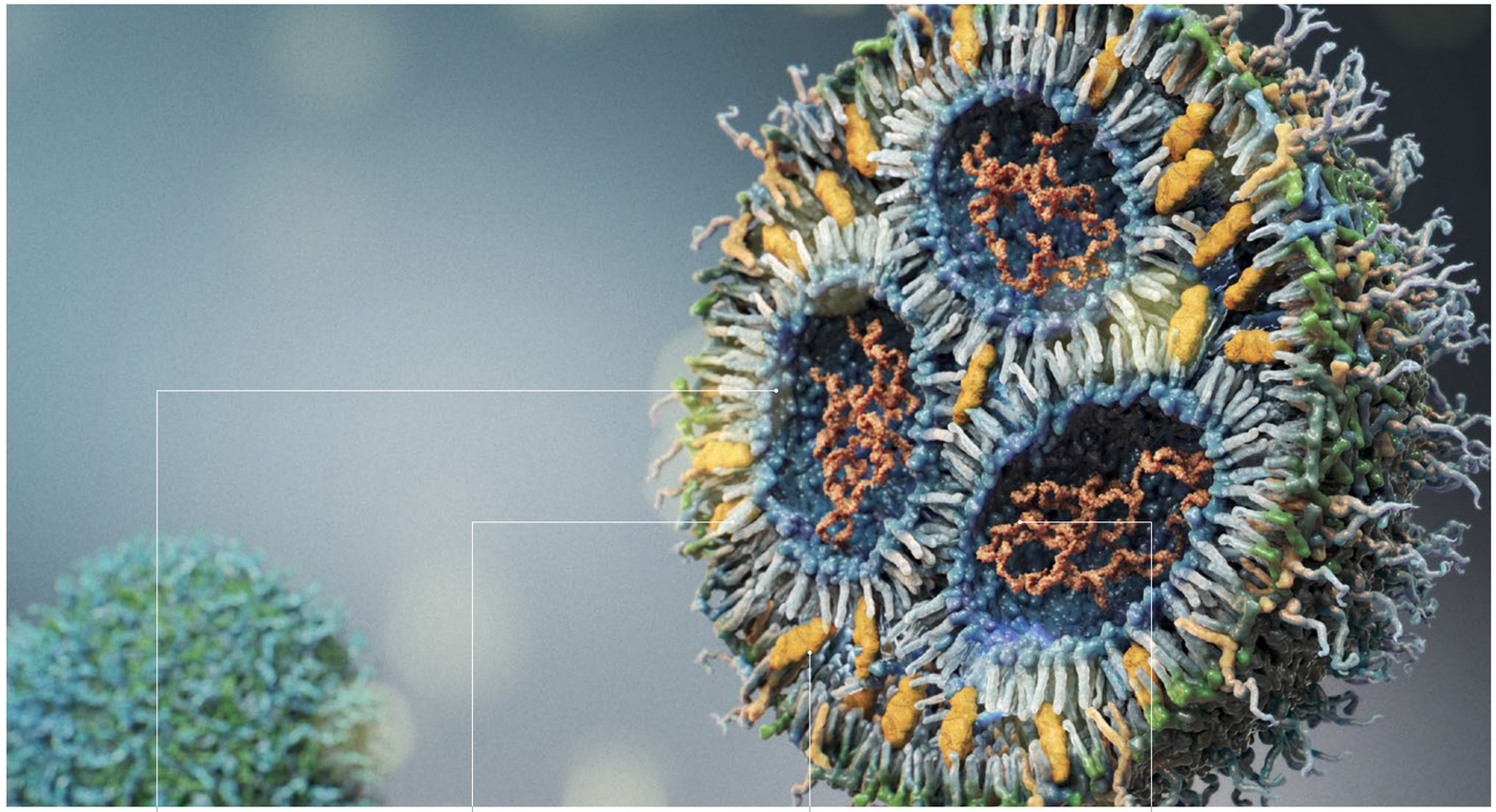
Discovered in the 1960s, mRNA has had a long lead time and was approved regulatorily for the first time as a vaccine in 2021.

For the large and fragile cargo to enter cells effectively, the delivery mechanisms needed to evolve, amongst other factors. Today, different in vitro transcribed RNA (IVT RNA) types, such as linear mRNA, large self-amplifying RNA (saRNA) or self-replicating RNA (srRNA), and circular RNA without 5' and 3' ends are approved for drugs or are in clinical phases. Their usage in medicine is highly diverse, as seen by their application in vaccines, gene editing, replacement therapy, and neoantigen expression. For any drug application, the comprehensive characterization of the large and often heterogeneous IVT RNA is critical.



"Given the "one break no effect" with mRNA, the integrity of mRNA drugs must be assessed to ensure its quality. Capillary gel electrophoresis (CGE) is a key tool in this field. CGE systems, such as the BioPhase 8800 system from SCIEX, offer high resolution and can efficiently characterize RNA profiles, enabling accurate quality control. Ensuring the integrity and purity of mRNA formulations is essential for the development of effective and safe therapeutics."

Jérémie Parot (PhD)
Research Scientist, SINTEF



mRNA integrity

Separate impurities from your IVT RNA and assess the integrity and purity of your product.

Circular RNA

Ensure separation of circular products from linear precursors and assess product purities.

poly(A) assessment with MS

Leverage LC-MS for the characterization of your mRNA 3' ends.

Encapsulation

Determine encapsulation efficiencies of mRNA in LNPs and simultaneously assess mRNA integrity.

saRNA and srRNA integrity

Break through boundaries for assessing purity and integrity of large RNA products beyond 9 kb.

5' end cap

Achieve identification and quantitation of capping structures and intermediates.

poly(A) assessment with CE

Characterize the poly(A) tail length and distribution of your IVT RNA with CE.

Protein expression

Identify and quantify expressed proteins and characterize PTMs of proteins.

Expert Q&A:

Adressing stability challenges of mRNA-LNPs

mRNAs are fragile molecules that are not meant to be very stable. Increasing their stability requires careful assessment of multiple factors. Here, Dr. Jingtao Zhang (Catalent® Pharma Solutions) provides his insights.

Can you provide details for the conditions of your pre-injection rinses?

Prior to starting a sample sequence, we perform an acid wash and a water wash and then fill the capillaries with gel. As part of our optimized method, we use 70 psi for 2 minutes for the acid wash, followed by a water wash at 70 psi for 2 minutes. To fill the capillaries with gel, we use 50 psi for 5 minutes. Once the capillaries are filled with gel, we run the separation method briefly—for 2 minutes—to pull out any small impurities before moving ahead to any samples. In addition to pre-injection rinses, we found it extremely important to use sample loading solution (P/N 608082) to dilute samples prior to injection. It helped us improve the peak shape and resolution of our mRNA samples and the RNA ladder.

Can you elaborate on your settings for the pressure injection of mRNA?

We used 1 psi for 5 seconds. However, you can adjust the duration depending on your needs. We have also used electrokinetic injection in the past, which applied -1.0 kV for 6 seconds to load samples into the capillaries. This method also worked well and required less sample, but we decided to stick with pressure injection since it provides higher reproducibility in our experience.

Is there a size limit for mRNA analysis on the BioPhase 8800 system?

I'm not aware of a specific size limit on the BioPhase 8800 system. The ladder from the RNA 9000 Purity & Integrity kit covers a range from 500 nt to 9,000 nt. While most mRNA we work with is within this range, larger mRNA can be analyzed when extending the run time, with the caveat of working outside of the calibration curve range which would impact sizing accuracy. This would be something interesting to investigate.

Which capillaries do you use for mRNA analysis?

The capillaries we used for the BioPhase 8800 system are bare-fused silica (BFS) capillaries as part of the BioPhase 8800 BFS capillary cartridge (P/N 5080121). The cartridge contains 8 pre-installed capillaries, each 30 cm long, and a detection window 20 cm from the inlet. Liquid-based temperature control of the separation temperature is incorporated with these cartridges.

Can you comment on the transferability of your extraction method with the Triton X-100 and temperature settings for CGE analysis to other mRNA products?

In general, the method can be transferred to different mRNA products. However, I suggest optimizing the surfactants and the temperature settings since different mRNA products can be more susceptible to secondary structure formation, aggregation, or formation of multimers, and may have different sensitivity towards temperature. You really want to make sure that your surfactant concentration is suitable for your mRNA product. In case you are getting poor recovery, you would want to investigate surfactant types or concentration. Since different mRNA products exhibit different sensitivities to temperature, I recommend optimizing sample incubation temperatures. For instance, a test range of 40 to 70 degrees Celsius, including different incubation times for a given temperature, is a good starting point. I also recommend optimizing your cartridge temperature as well to reduce the formation of secondary structures.

Did you find that the recovery of mRNA from your LNPs is dependent on the type of ionizable lipid used?

We tried several types of ionized lipids and different compositions of LNPs. For the ones we tried, we have not experienced significant issues related to recovery using an optimized extraction method. We did observe that non-optimized extraction methods, including sample preparation such as surfactant level and denaturants, could affect recovery.

Are you able to comment on other approaches regarding stability, such as lyophilization?

The approach we currently take is focused on preserving the formulation through freezing. This adds inconvenience and increases costs. During lyophilization, water is removed from the LNP system, and a product can be stored in refrigerated conditions, potentially even at room temperature. The requirements for upholding a suitable cold chain would be dramatically reduced. Alternative solutions for storage of mRNA products, like lyophilization, are therefore very interesting. A lot of work still needs to be done, particularly regarding lyophilization of LNPs.

Can you comment on how excipients affect mRNA integrity?

Various excipients—lipid and non-lipid excipients—play an especially important role in stabilizing the overall product and can also affect the active ingredient, the mRNA. For instance, it is known that secondary structures of mRNA are pH dependent. Excipients, such as buffer salts, that modulate the pH can therefore affect the mRNA structure. Lipid excipients are crucial to the drug's efficacy and tolerability. As a result of this and stability concerns, we need to pay a lot of attention to their quality. Impurities in excipients can lead to degradation of mRNA. A now well-known example is the reaction of mRNA with aldehydes, which can exist as impurities in lipids. When evaluating excipients, my suggestion is to decouple the effects of the excipients from those related to the excipients' quality.

Is there any carrier system being used for mRNA other than LNPs?

Up until now, LNPs leveraging ionizable lipids are the most clinically validated system for mRNA delivery. LNPs come in different flavors, usually using ionizable or cationic lipids as a key component, and can complex the negatively charged mRNA cargo. Some LNP research focuses on the usage of biodegradable lipids to improve the biocompatibilities while others have focused on targeted systems for enhanced efficiencies. Other systems can be used for non-viral delivery, such as polymers or cell-penetrating peptides (CPP). In some cases, polymeric systems can be coupled with LNPs to gain the best of both worlds. It's an exciting field with a lot of ongoing research.

Read Q&A blog

Dr. Jingtao Zhang is the Scientific Director of the Biologics Group at Catalent® Pharma Solutions. He is responsible for developing new technical capabilities and product solutions to solve clients' pressing pharmaceutical problems with a special focus on expanding mRNA-LNP within Catalent Pharma Solutions. He has more than 16 years of experience in R&D and commercialization of small molecules, peptides, oligonucleotides, biologics and mRNA-LNP drug products in pharmaceutical and CDMO settings. Jingtao received his PhD in Chemical Engineering from the University of Wisconsin-Madison and authored/co-authored more than 30 articles in peer-reviewed journals.

mRNA integrity and purity

The stability of fragile RNA cargo requires careful testing during development because mRNA-based drugs can lose their efficacy when truncated. In addition, process-related nucleic acid impurities may pose safety concerns. The integrity and purity of mRNA constructs are therefore important aspects for product quality. High-resolution separation with excellent reproducibility enables the assessment of these product quality parameters accurately and reliably.

- Break through analytical boundaries with ultra-high resolution and excellent reproducibility
- Determine the integrity and purity of your nucleic acid products from 50 up to 9,000 nucleotides (nt) and beyond
- Confidently transfer assays from development to QC and streamline data management through compatibility with data management systems

Confirm integrity and determine purity with excellent resolution and reproducibility

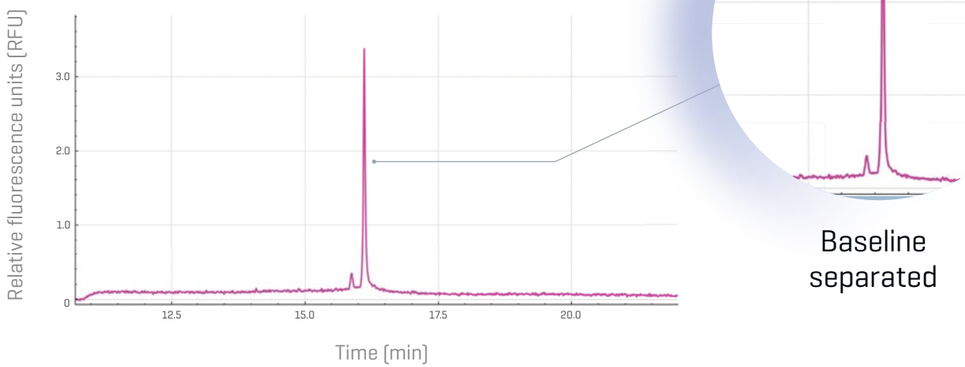


Figure 29: Electropherogram of mRNA extracted from an LNP analyzed using the BioPhase 8800 system. The mRNA of 1.929 kb was encapsulated in an LNP with MC3 as the ionizable lipid.

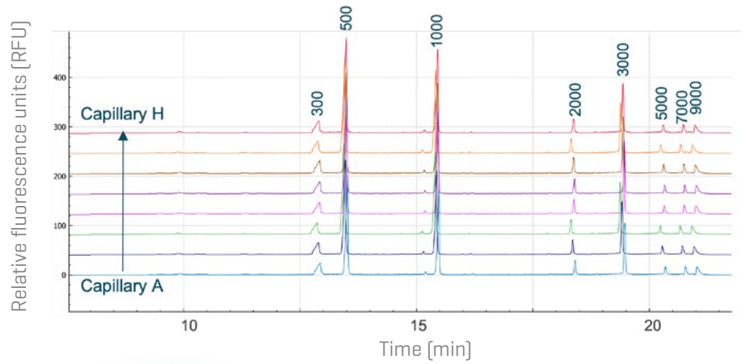


Figure 30: Reproducibility across all 8 capillaries of the BioPhase 8800 system. The electropherograms of the single-stranded ladder, spanning from 150-9,000 nt, show full separation and excellent reproducibility for the entire size range of the ladder from the RNA 9000 Purity & Integrity kit.

RNA 9000 Purity & Integrity kit

An intuitive kit to assess RNA and ssDNA integrity, purity, and size, compatible with BFS capillaries.

Learn more

Discover more details in the technical note about mRNA integrity and purity assessment

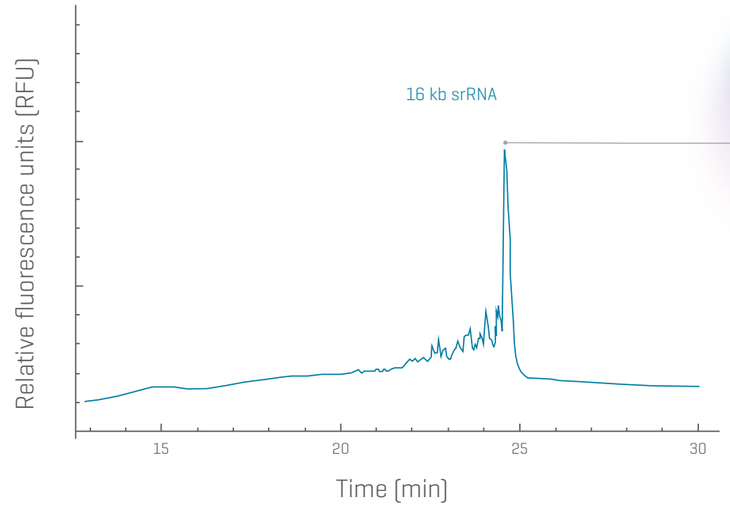
Read technical note

srRNA integrity and purity

Conventional mRNA and base-modified mRNA (bmRNA), which incorporates chemically modified nucleotides, are non-replicating IVT RNAs. SrRNA is an emerging third type that is based on an engineered viral genome, devoid of viral structural protein genes. The self-replicating ability makes srRNA a promising tool for new therapeutic drugs, despite challenges with its length.

- Determine the integrity and purity of your srRNA even beyond 9,000 nt
- Break through analytical boundaries with ultra-high resolution and excellent reproducibility
- Confidently transfer assays from development to QC and streamline data management through compatibility with data management systems

Confirm integrity and monitor impurity profiles with high resolution and reproducibility



16 kb
well resolved

Figure 31: Electropherogram of research-grade srRNA material (16 kb) obtained from Replicate Bioscience, San Diego, CA, USA.

Discover more details in the technical note about srRNA integrity and purity assessment

Read technical note

Circular RNA assessment

Circular RNAs are next-generation IVT RNAs that provide the benefit of high resistance towards exonucleases—without 5′ caps or poly(A) tails. To achieve circular RNAs, linear precursors are chemically or enzymatically ligated. Understanding the purity of the circular product requires a high-resolution separation workflow, which can separate linear precursors, degradation, and high molecular weight products from the desired circular RNA.

- Take charge of your product quality and determine the efficiency of your circulation processes
- Break through analytical boundaries with ultra-high resolution and excellent reproducibility
- Confidently transfer assays from development to QC and streamline data management through compatibility with data management systems

Full separation of linear precursor and circular RNA

Fully separate linear precursors from circular RNAs with the highest reproducibility

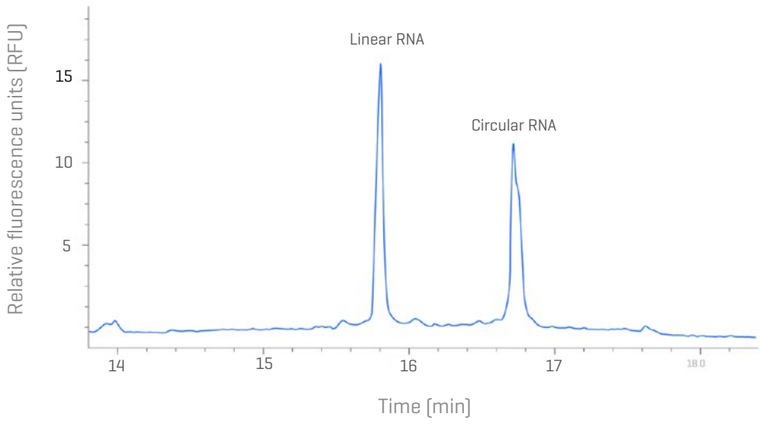


Figure 32: Separation of circular from linear precursor RNA with CGE-LIF. The linear RNA product migrates faster through the gel matrix than the circular RNA product due to a smaller effective cross-section.

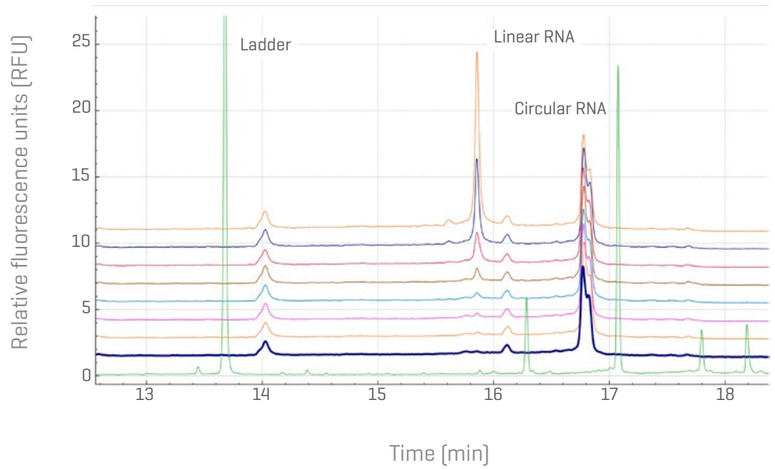


Figure 33: Sensitivity assessment for linear RNA impurity. The circular RNA product was spiked with a serial dilution of linear precursor. A detection limit of 0.1% relative to the circular product was determined. Green trace: ssRNA ladder from RNA 9000 Purity & Integrity kit.

Break through analytical boundaries with ultra-high resolution and excellent reproducibility

Discover more details in the technical note about circular RNA assessment

Read technical note

Encapsulation efficiency of mRNA

LNPs are designed to keep the fragile genetic cargo safe. Degradation and loss of function of nucleic acids is accelerated if they are not sufficiently encapsulated. In addition, the cellular uptake of the drug can be impeded. The encapsulation efficiency of the genetic cargo is, therefore, an important quality to be optimized and monitored during the development of LNP-based drugs.

- Take charge of development decisions by understanding encapsulation efficiencies of drug substances with a reliable kit-based CE workflow
- Determine free and encapsulated mRNA amounts with excellent repeatability and sensitivity
- Simultaneously monitor degradation products in your samples leveraging exceptional resolving power

Achieve it all:

- Excellent resolution
- Sensitivity
- Linearity with low %CVs

Achieve it all: Excellent resolution, sensitivity, and linearity with low %CVs

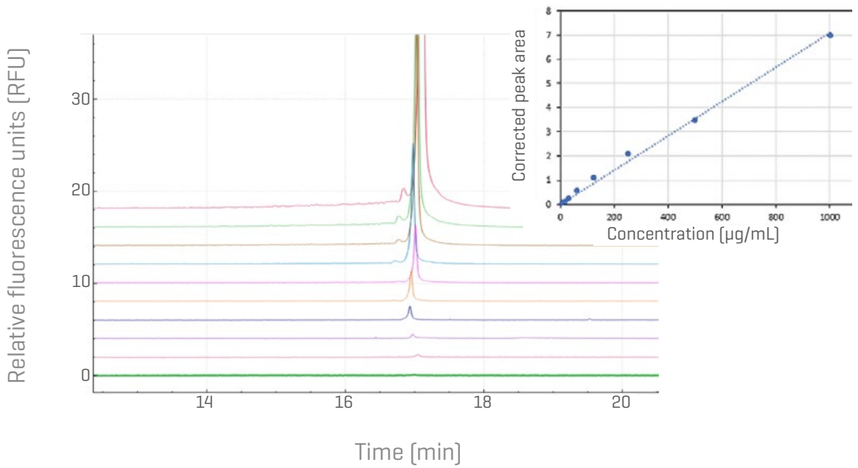


Figure 34: Serial dilution of mRNA standard. Electropherograms show excellent migration time reproducibility. Corrected peak area vs. mRNA concentration showed a linear correlation with $R^2 = 0.9989$.

Nominal (µg/mL)	Measured (µg/mL)				%CV	Accuracy (%)
	#1	#2	#3	Mean		
400	387	390	382	386	1.1	97
500	494	489	480	489	1.7	98
600	574	580	570	575	0.9	96

Figure 35: Results of replicate injections of different mRNA concentrations. Reproducible peak areas with very low %CV and very high accuracy were determined based on triplicates.

Reproducible peak areas with very low %CV and very high accuracy were determined based on triplicates.

Discover more details in the technical note about mRNA encapsulation efficiency analysis with CE

Read technical note

5’ capping analysis

The 5’ cap of IVT mRNA has a direct impact on its stability and translation efficiency and is therefore considered a CQA. Since G cap, cap 0, and the mature cap 1 are linked to different pharmacological efficacies, detailed characterization and simultaneous relative quantitation is needed to ensure product quality. The differences between the different capping structures are only 1-2 methyl groups, which requires high resolving power to be distinguished.

- Characterize 5’ caps and intermediate products reliably using excellent time-of-flight (TOF) MS data quality
- Obtain relative quantitative information automatically or tailor quantitative calculations specifically to your needs
- Take back your time with intuitive acquisition and processing software

Take back your time with intuitive acquisition and processing software

Understand your product quality with ease using high-quality data

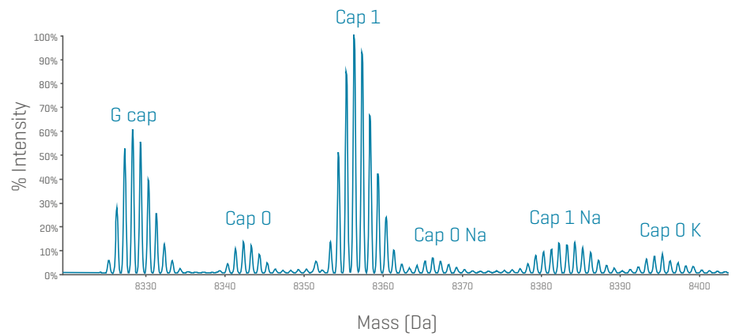


Figure 36: Deconvoluted data for mRNA 5’ end with isotopic resolution. Different capping intermediates and mature cap 1 species as well as sodium (Na) and potassium (K) adducts were identified.

	Name	Neutral Mass	Peak Area	% Area
1	Capped - ppUncap	7980.17	8.84E+05	34.57
2	Gcap	8325.24	5.62E+05	21.96
3	Cap1	8353.27	4.02E+05	15.73
4	Capped - pUncap	7900.21	3.21E+05	12.53
5	ppp Uncap K+ adduct	8098.06	1.38E+05	5.41
6	ppp Uncap	8060.13	1.22E+05	4.79
7	Cap0	8339.27	7.12E+04	2.78
8	ppp Uncap Na+ adduct	8082.13	3.32E+04	1.30
9	Capped - ppUncap Na+ adduct	8002.17	2.12E+04	0.83
10	Capped - ppUncap K+ adduct	8018.13	2.24E+03	0.09

Figure 37: Results of identified mRNA capping moieties. Table shows identified species, associated molecular weight, and relative quantitative information.

Learn more

Read technical note

3’ end poly(A) tail of mRNA with LC-MS

Polyadenylation is needed to enable product stability and translation efficiency of mature mRNA products. As a result, the length and distribution profile of the poly(A) tail during development are highly relevant concerns, whether the tail is template-encoded, enzymatically added, or applied through a combination of these approaches. The detailed characterization of poly(A) tails requires accurate data with high resolving power.

- Leverage excellent data quality through exceptional negative ionization efficiency and declustering of adducts with state-of-the-art source design
- Uncover relevant information on poly(A) tails, such as molecular weight and distribution profiles
- Trust in your high-resolution results with great mass accuracy

Dig deeper into your product quality with high-quality data

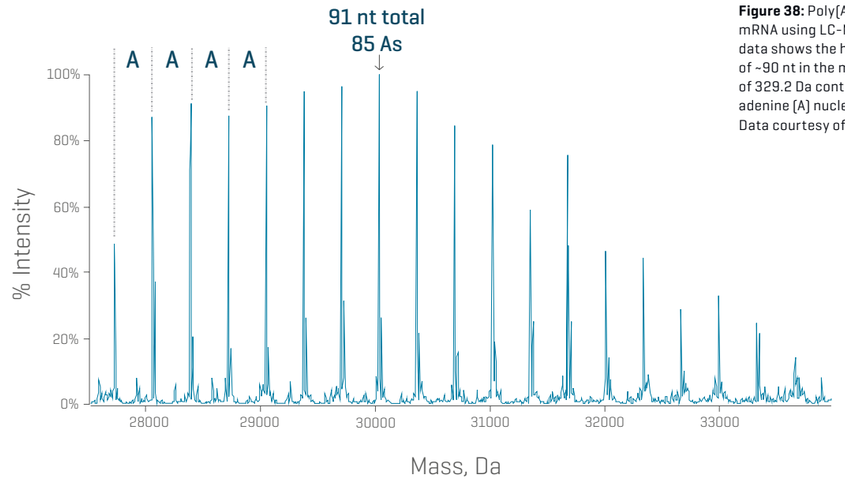


Figure 38: Poly(A) tail analysis from digested mRNA using LC-MS. Deconvoluted TOF-MS data shows the heterogeneity of the tail length of ~90 nt in the mRNA sample. Each Δ amu of 329.2 Da contributes to the addition of 1 adenine (A) nucleotide in the polynucleotide. Data courtesy of Phenomenex, CA, USA.

More questions?

Contact us

3’ end poly(A) tail of mRNA with CGE-UV

Since the 3’-end poly(A) tail is a CQA affecting product stability and translation efficiency, its optimization and monitoring throughout development and manufacturing is critical. The determination of length and distribution profiles requires accurate assays with high resolving power and repeatability. To enable implementation in QC environments, intuitive and robust assays are needed.

- Take control of your IVT RNA 3’ CQA with reproducible, high-quality CE data
- Dig deeper than ever before into the dispersity of your 3’ poly(A) tails with single-nucleotide resolution
- Confidently transfer assays from development to QC and streamline data management through compatibility with data management systems

Enable yourself with single-base resolution and excellent reproducibility

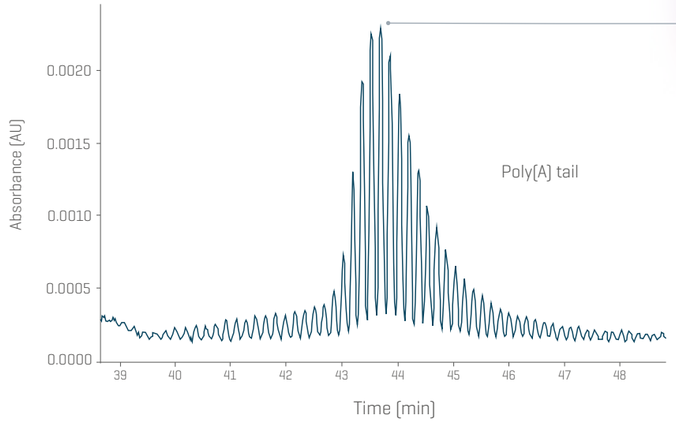
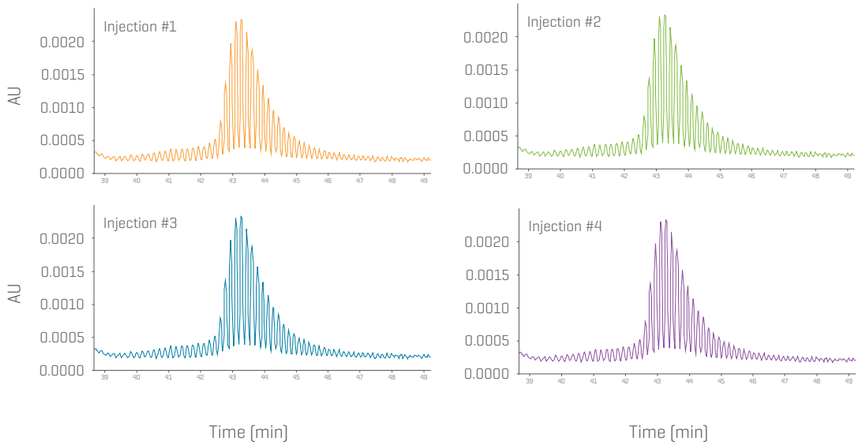


Figure 39: Poly(A) tail analysis from mRNA with CGE-UV. Electropherogram shows single-base resolution of mRNA poly(A) tails with most abundant species of 121 nt in length.

Figure 40: mRNA poly(A) tail reproducibility analysis with CGE-UV. The 4 replicate injections show high reproducibility in terms of migration time and peak profiles.

Dig deeper than ever before into the dispersity of your 3’ poly(A) tails with single-nucleotide resolution



Discover more details in the technical note about poly(A) tail analysis with CGE

Read technical note

Protein expression analysis

Upon successful delivery of the genetic cargo, drug substances such as IVT RNA are supposed to induce protein expression. While ELISAs and western blots are widely used to determine functional potency, these assays are limited by the availability of antibodies with high specificity for the target protein. Flexible approaches to determine protein expression that do not rely on antibodies can help with adhering to timelines and fast-paced changes in development pipelines.

- Break through the boundaries of complex matrices and achieve reliable identification and excellent quantitation simultaneously
- Leverage impeccable quantitative performance for decision making with high linear dynamic range and low limits of detection and quantitation
- Streamline your quantitative data processing with state-of-the art-software

Don’t let matrices hold you back. Gain signal-to-noise with high resolution quantitation.

Don’t let matrices hold you back—level up your MS/MS sensitivity

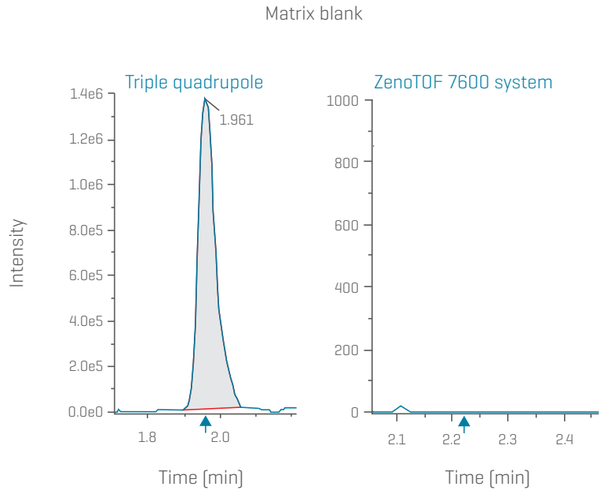


Figure 41: Comparison of matrix blanks. Same matrix blank was injected into a triple quad system and the ZenoTOF 7600 system. The high resolution on the TOF system resulted in a clean blank and, therefore, lower limits of quantitation for a peptide analyte compared to the triple quad data obtained.

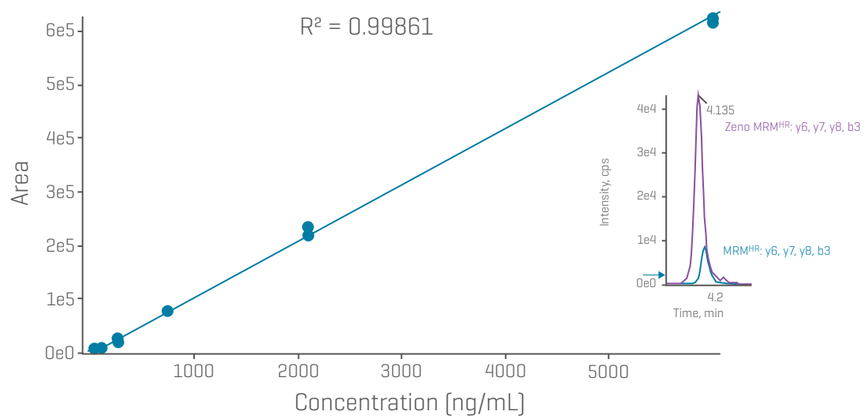


Figure 42: Peptide quantitation in complex matrix. Calibration curve obtained for a peptide in complex matrix using the sum of multiple fragment ions enhanced by the Zeno trap. Inset shows a comparison of peak intensities obtained when summing the same peptide fragment ions with the Zeno trap enabled (pink) and without (blue).

Increase fragment intensities with the Zeno trap

Discover more details in the technical note about peptide quantitation in matrix

Read technical note

Analytical solutions for IVT RNA

Suitable for:

- High-quality separation
- Rapid method development and sample analysis

BioPhase 8800 system

Purpose-built for achieving high quality data efficiently across various analytical assays.

Learn more

RNA 9000 Purity & Integrity kit

An intuitive kit to assess RNA and ssDNA integrity, purity and size, compatible with BFS capillaries.

Learn more

BFS capillary cartridge

A pre-assembled bare-fused silica 8-capillary cartridge available in 30 and 50 cm total length.

Suitable for:

- High-quality separation
- Single nucleotide resolution for poly(A) 3’–ends
- Large srRNA assessment

PA 800 Plus system

A solution enabling confident decision making and QC-readiness for your biopharmaceutical products.

Learn more

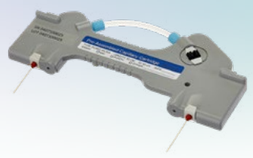
RNA 9000 Purity & Integrity kit

An intuitive kit to assess RNA and ssDNA integrity, purity and size, compatible with BFS capillaries.

Learn more

BFS capillary cartridge

A pre-assembled bare-fused silica single capillary cartridge available in 30 cm total length.



ssDNA 100-R kit

Designed for ultra-high resolution analysis of single-stranded nucleic acids using coated capillaries.

Analytical solutions for IVT RNA

Suitable for:

- 5’ cap and poly(A) 3’–end characterization
- Robust, analytical flow setup

ExionLC AE system

An LC system that seamlessly integrates with your SCIEX MS for reproducible data, batch after batch.

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X500B QTOF system

An intuitive QTOF system, designed to facilitate everyday biologic characterization assays.

Learn more

Biologics Explorer software

A powerful software tool to support LC-MS/MS protein and oligonucleotide characterization assays.

Learn more

SCIEX OS software

The next generation of operating and processing solution for an enhanced LC-MS/MS analysis experience.

Learn more

Suitable for:

- 5’ cap and poly(A) tail characterization
- Protein expression analysis
- High flexibility to perform a range of additional workflows

ExionLC AE system

An LC system that seamlessly integrates with your SCIEX MS for reproducible data, batch after batch.

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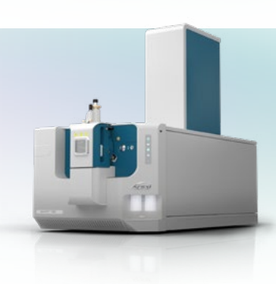
ZenoTOF 7600 system

A high-resolution solution, combining powerful MS/MS sensitivity and alternative fragmentation technology.

Learn more



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Cytiva

Cytiva is a global leader in technologies, solutions, and services for the development of LNP-delivered genomic medicines, including mRNA vaccines and therapeutics.

Our portfolio, combined with deep expertise in LNP formulations, accelerates drug programs to clinics and beyond.

Nano Assemblr™ platform
Reproducible LNP production scalable from bench to clinic

Ionizable lipids
A library of LNP formulations available for all stages of drug development

BioPharma Services
One-stop-shop solution for formulation, process, and analytical development with clinical LNP manufacturing

Cytiva. validated technologies increase stability, efficacy, yield, and quality of LNP delivered genomic medicines and lower the barrier to develop these important nanomedicines, accelerating timelines from concept to clinic.

Phenomenex

Phenomenex is a global technology leader committed to developing novel analytical chemistry solutions that solve the separation and purification challenges of labs that support the entire lifecycle of biotherapeutic modalities.

Incorporating expertise and knowledge through collaborations with our customers, we've put forth a solution portfolio designed specifically to address common challenges associated with modern biopharmaceutical analysis.

The Biozen™ Oligo LC column brings a unique combination of core-shell versatility and high pH ruggedness necessary for oligonucleotide separations. The Biozen Oligo column is packed in a unique bio-inert titanium hardware designed to minimize sample loss and adsorption issues typically seen with stainless steel hardware, demonstrating improved recovery and peak shape.

Learn more about Phenomenex biopharmaceutical product solutions and how we can help support your next project here.

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SCIEX Now

- Manage your instruments.
- Submit and manage support cases, track status, and view history.
- Access online training courses and articles.
- Manage software licenses linked to your registered instruments.
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SCIEX Now learning hub

- SCIEX Now learning hub success programs provide LC-MS and CE training customized to meet your exact needs.
- With a selection of training methods and certifications available, you can build a mass spectrometry program that is most suited to your lab and users.
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