Inspired by nature combined with cutting-edge technology

Analytical solutions for the development of superior viral vector-based drugs

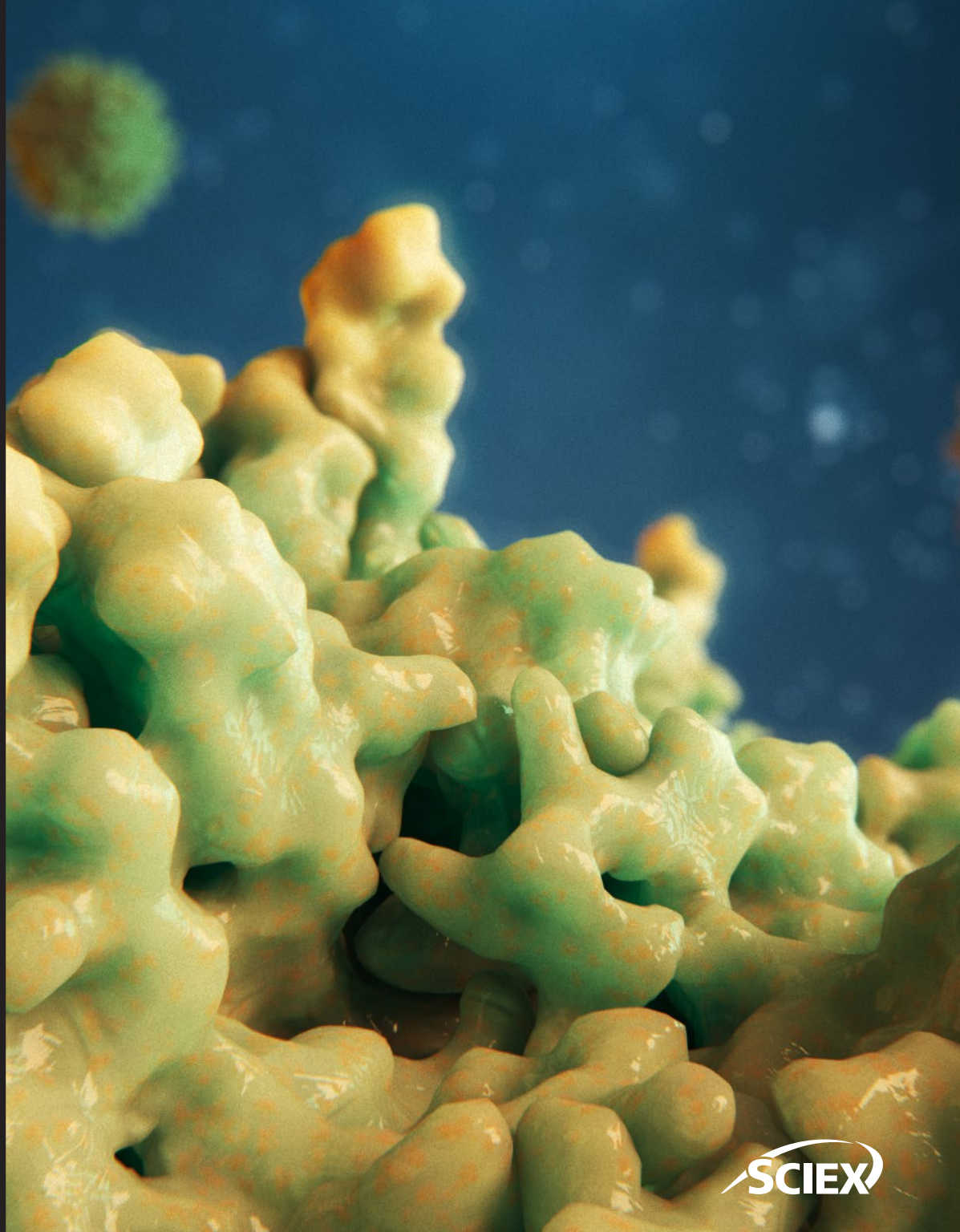
SCIEX

The Power of Precision

The development of viral vector vaccines and therapeutics means overcoming many challenges.

Using intuitive, innovative and informative analytical solutions to characterize viral carriers and achieve safe and effective drugs lets you stay focused.

Work with an evolving partner to realize the full potential of using viral vectors based on adenoviruses (AVs), adeno-associated viruses (AAVs), lentiviruses (LVs) and virus-like particles as delivery vehicles for nucleic acid-based gene therapies and vaccines.



Gain insights into critical quality attributes (CQAs) of viral vectors

Plasmid DNA topology

Plasmid DNA (pDNA) provides encoding for the virus and desired transgene and is used for generating packaging cells. Functional pDNA needs to be supercoiled, and its quality is important to optimize viral vector titers.

Viral proteins

Non-enveloped viruses have a protein capsid that interacts with the host cells. Protein integrity and purity, the protein sequence and post-translational modifications (PTMs) are important aspects that can impact vector potency.

Viral genome

Different viral vectors have various types of genomes. Vector potency, immunogenicity and transduction efficiency are impacted by the integrity and purity of the viral genome, which must be characterized.

Full-and-empty ratio

Only viral vectors with intact genomes (full) can be effective delivery vehicles. Understanding the amount of full particles is crucial for product quality.

Residual host cell nucleic acids

Residual host cell DNA and RNA are process-related impurities that can negatively impact vector potency and immunogenicity. Determining their size in relation to their quantity is crucial to product safety and efficacy.

Host cell proteins

The safety and efficacy of viral vector products can be impacted by proteins derived from packaging cells. The diverse landscape of packaging cell lines and the need to combat future pandemics with unprecedented response times require highly adaptable solutions for confidently identifying process-related impurities in viral vector products.

Proteome profiling

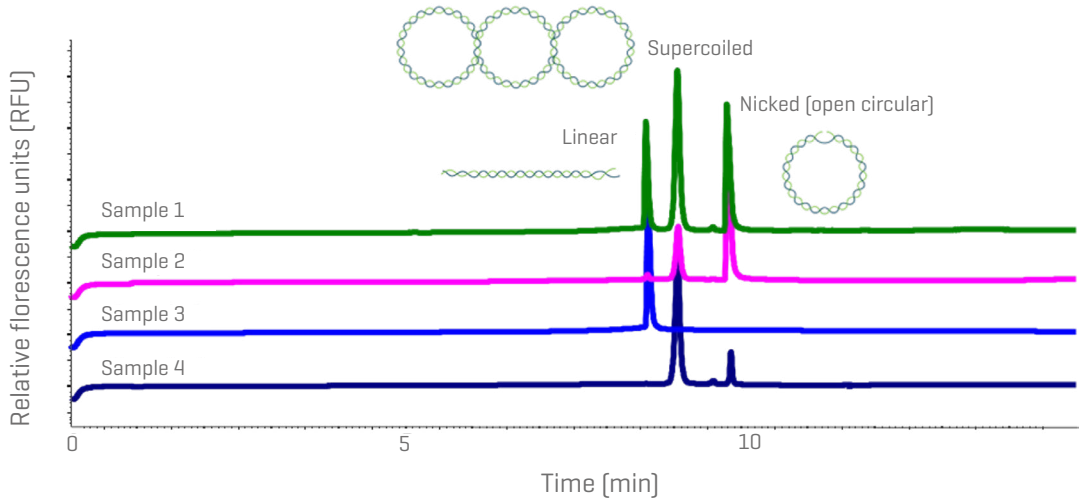
Editing a specific gene and its expression with a viral vector can have various effects on the entire proteome, which need to be understood.

The starting point: plasmid DNA

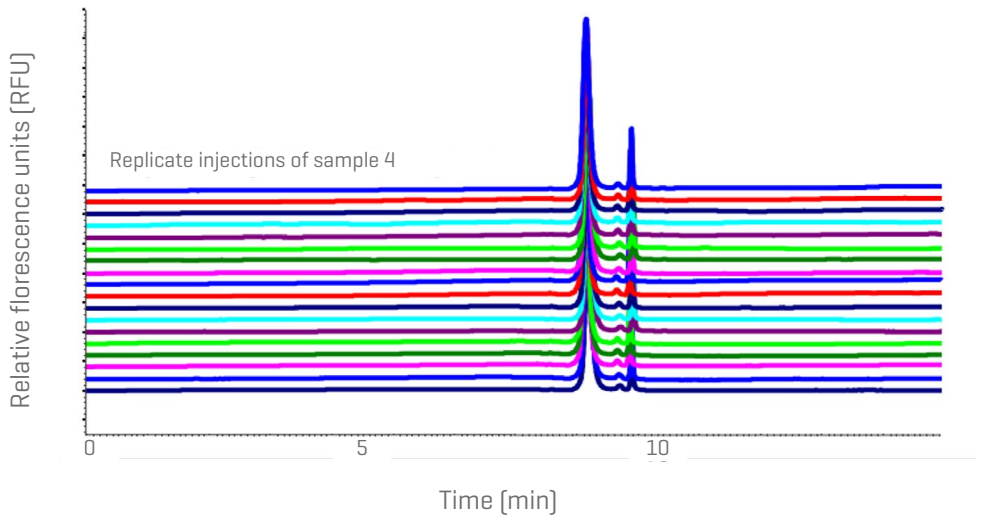
Gene therapy applications and vector-based vaccines need high-quality intermediate products, such as plasmid DNA (pDNA), in large quantities. Modern approaches for viral vector production use triple transfection of plasmids into packaging cell lines. Scale up of pDNA can result in challenges related to the homogeneity of supercoiled plasmids, which are needed for successful viral production.

- Rely on the baseline resolution of different topological variants when working with pDNA using the **PA 800 Plus system** and the dsDNA 1000 kit
- Achieve the highest sensitivity for early-stage development samples with laser-induced fluorescence (LIF) detection
- Confidently transfer assays to QC with the highest precision and robustness using the **PA 800 Plus system**
- Streamline data management through compatibility with the Empower Chromatography Data System (CDS) from Waters

Differentiate different topological plasmid variants



Rely on a high-resolution method with optimal reproducibility



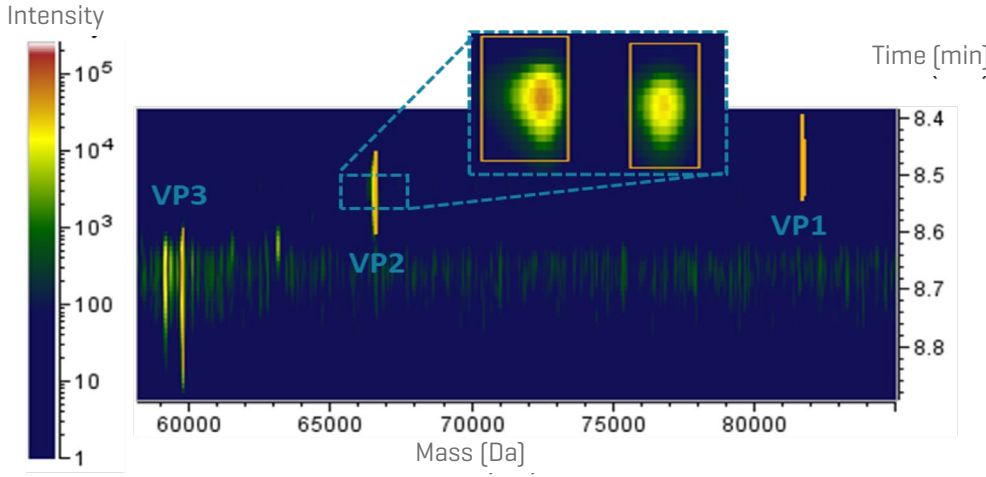
sciex.com/plasmid-analysis

Intact viral protein characterization

With AAVs, 3 viral proteins (VPs) build the capsid. In the case of non-enveloped viruses, the capsid is directly interacting with the host cells. Hence, integrity and post-translational modification (PTM) profiles of VPs are important quality criteria that can affect viral uptake. Chromatographic separation of VPs can be difficult to achieve, however, due to their similar physical properties. In addition, low- abundance protein impurities can be missed.

- Set new frontiers for intact protein and impurity characterization with 3D visualization options for deconvoluted data in Biologics Explorer software
- Ensure the integrity of your capsid proteins with excellent accurate mass data obtained with the X500B QTOF system or the ZenoTOF 7600 system
- Obtain relevant information on identities and more accurate quantities for PTMs based on time-resolved (3D) deconvolution in Biologics Explorer software
- Get started on high-quality data acquisition quickly and confidently with intuitive SCIEX OS software

Obtain more information more easily with deconvolution heat maps



Access accurate quantitation of 3D deconvoluted data

Quantities

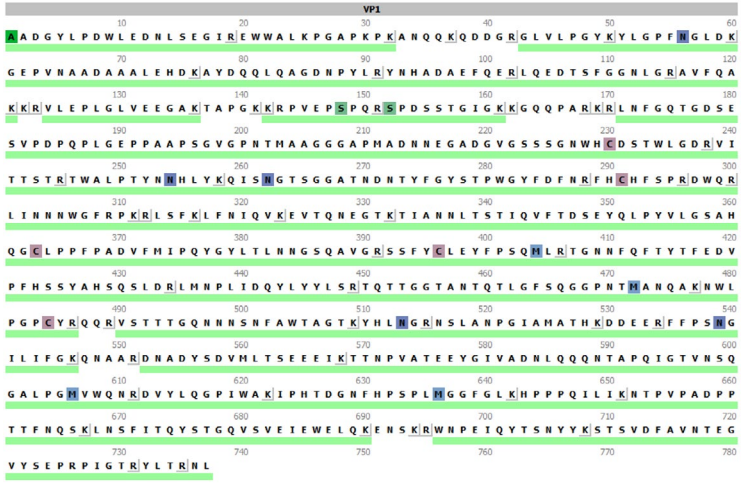
Protein	Avg. Mass	RT	Volume	Volume [%]
V1 + Acetyl	81666.5	8.46052	1152.98	0.191584
V1 + Acetyl + Phospho	81746.8	8.46571	147.446	0.0245004
V2	66517.2	8.51561	24419.6	4.05768
V2 + Phospho	66597.3	8.52536	15914.9	2.6445
V3 + Acetyl	59804	8.66032	560177	93.0817

Amino acid sequence and post-translational modifications

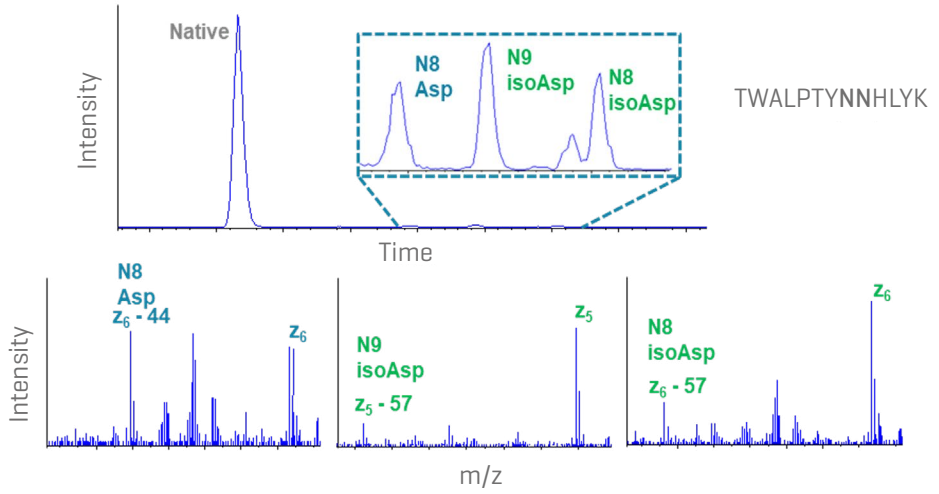
Confirmation of the sequence and identification of low-abundance PTMs require a deeper look into the viral proteins. A peptide-mapping approach can provide information on product quality attributes (PQAs) and critical quality attributes (CQAs). Low sample amounts, however, are a challenge for analytical assays. Additional challenges include the identification of deamidation-derived isomers and fragile PTMs that can affect the charge heterogeneity and, as a result, viral uptake.

- Obtain high protein sequence and fragment coverage despite limited sample quantities with highly sensitive, high-resolution data acquisition
- Identify PTMs and their locations—including glycosylations, sulfations and phosphorylations—with the accurate mass **X500B QTOF system** and **ZenoTOF 7600 system**
- Break through boundaries by overcoming the challenges of differentiating amino acid isomers and localizing fragile PTMs with electron activated dissociation (EAD), an intuitive alternative fragmentation technique available on the **ZenoTOF 7600 system**
- Take back your time with reliable processing using **Biologics Explorer software**

Trust in your protein sequences with high MS/MS coverage



Fully understand and localize challenging PTMs



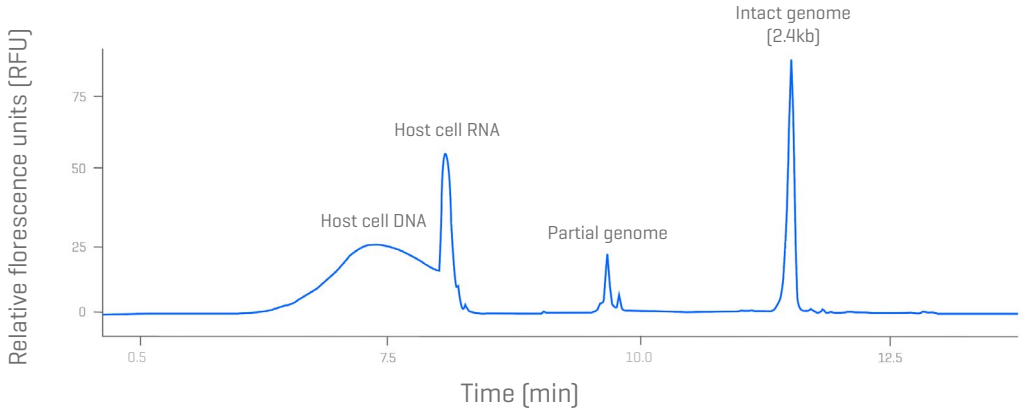
sciex.com/viral-vectors

Genome integrity

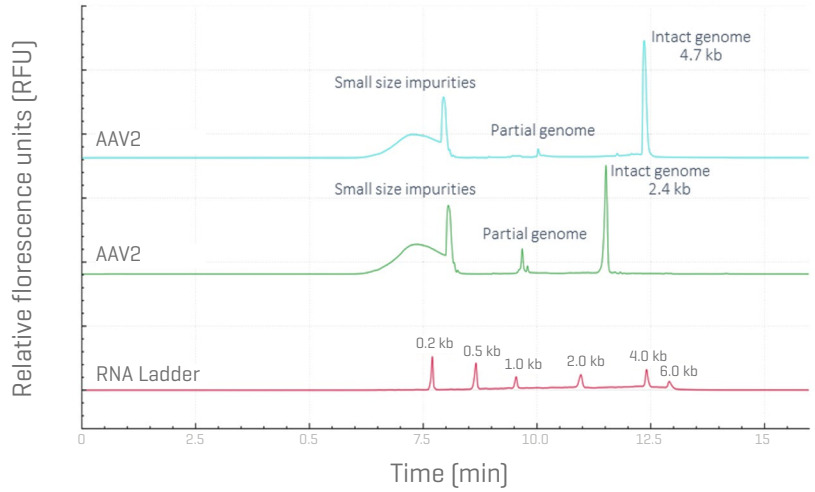
The integrity and purity of the viral genome are CQAs that impact vector potency, immunogenicity and transduction efficiency, and for this reason they must be characterized. However, the limited sizing capabilities of some analytical methods, such as PCR-based methods, can pose challenges for assessing the entire viral genome, especially for assessing viruses with larger genetic cargo, such as lentiviruses or Coxsackie viruses. Furthermore, distinguishing between product-related impurities, such as degraded genomes and intact genomes, and ensuring their accurate quantitation can be challenging.

- Reach new milestones to confidently determine genome integrity, genome titer and impurities using the high separation power of the **BioPhase 8800 system** and the **PA 800 Plus system**
- Run your high-quality analyses smoothly and reproducibly with a kit-based turnkey solution using the **RNA 9000 Purity & Integrity kit**
- Simplify viral vector genome analysis by avoiding lengthy assay adjustments with a workflow suitable across serotypes and viral vectors
- Cover your data management needs through compatibility with the Empower

Assess genome integrity and nucleic acid impurities



Take back your time with a platform method across serotypes



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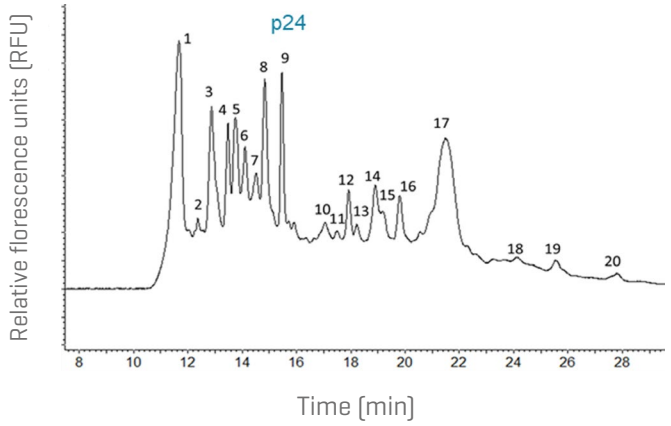
Protein profiling

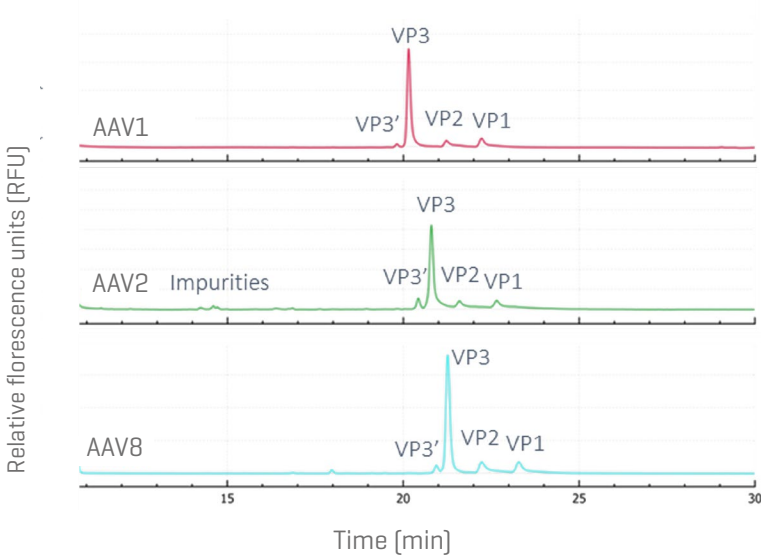
Viral vector characterization for vaccine and therapeutic drug development includes assessing the viral proteins. While MS-based solutions can provide molecular weight, sequence confirmation and insights into PTMs, other methodologies are needed to obtain relevant information on purity and to facilitate the transfer into regulated environments. High resolving power, throughput capabilities and reproducibility are important factors for these assays.

- Determine protein-based titer with confidence and understand protein profiles and impurities using the high separation power for viral proteins provided by the **BioPhase 8800 system** and **PA 800 Plus system**
- Reclaim your time with faster method development and the ability to run larger sample batches with the 8-capillary **BioPhase 8800 system**
- Avoid lengthy assay adjustments with a kit-based protein profiling workflow suitable across serotypes and viral vectors using the CE-SDS Protein Analysis kit
- Be covered for your data management needs through compatibility with the Empower CDS

Understand the protein changes of complex lentiviral vectors



Rely on a platform solution suitable for different serotypes



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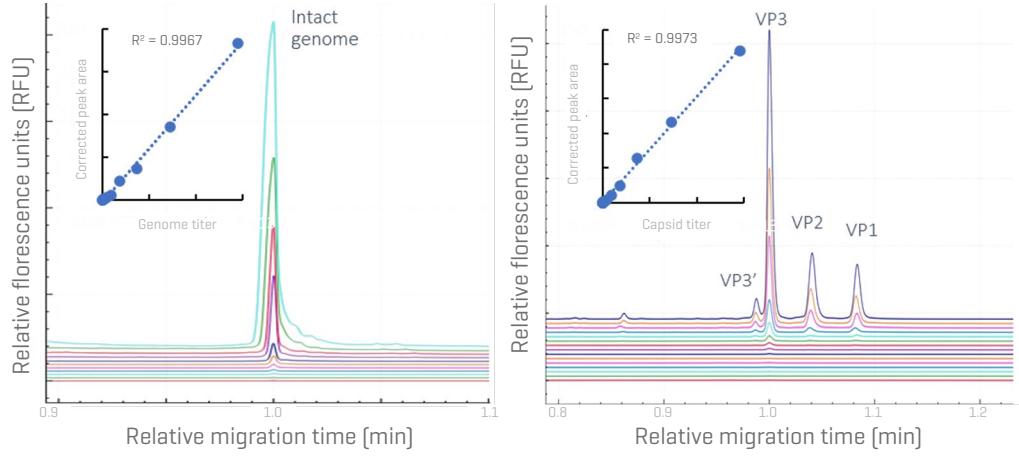
Full-and-empty ratios

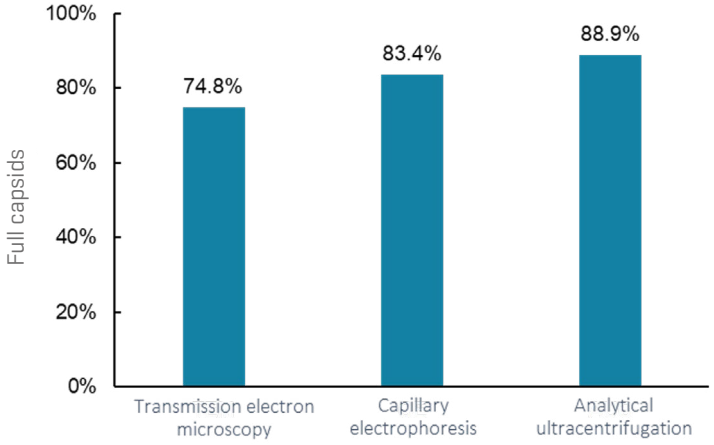
In addition to characterizing the genome and viral proteins, assessing the ratio of capsids with an intact genome (full capsids) vs. partial or empty capsids is necessary for comprehensive viral vector characterization. A variety of methods exist to determine this CQA, but the assays can have limitations. For example, some assays are cumbersome, must be adjusted for each serotype or require high levels of expertise, and some provide limited understanding of partially filled capsids.

- Take back your time by assessing multiple CQAs with high-quality data on a single platform using the BioPhase 8800 system or the **PA 800 Plus system**
- Determine genome integrity, capsid proteins and full-and-empty ratios, including partial capsids with serotype-independent workflows
- Simplify vector analysis with kit-based solutions using the RNA 9000 Purity & Integrity kit and the CE-SDS Protein Analysis kit
- Cover your compliance needs through compatibility with the Empower CDS

Assess genome integrity and nucleic acid impurities



Take back your time with a platform method across serotypes



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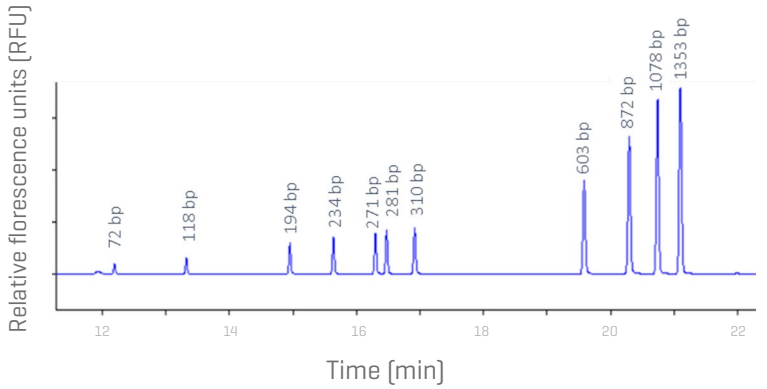
Residual host cell DNA

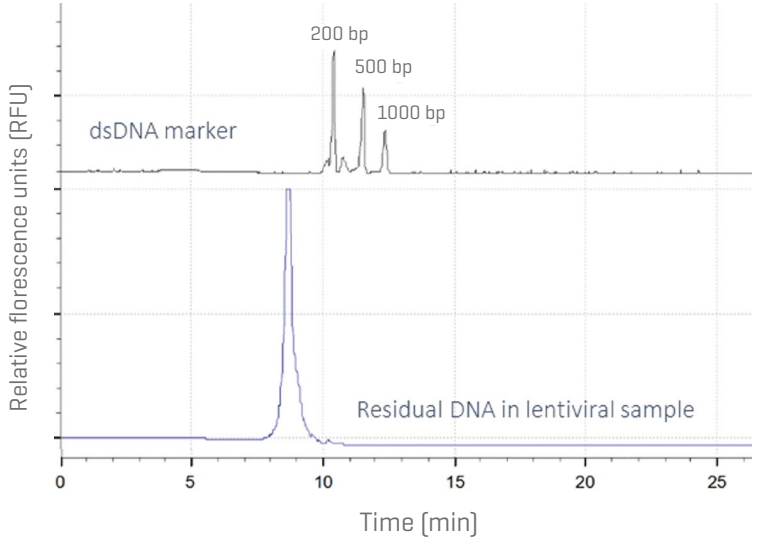
Host cell DNA, which is a process-related impurity, can be present in cell culture-derived vaccines and therapeutic products. Due to shearing during production, varying sizes of residual DNA might be present in a product. Since DNA with >200 base pairs (bp) could encode for undesired proteins, reliable size determination and simultaneous quantitation are crucial for product safety. Challenges arise for risk assessment if only DNA quantity is determined without information on sizes.

- Determine quantities and sizes of residual host cell DNA in your product with high resolving power using the **PA 800 Plus system** and the dsDNA 1000 kit
- Set new frontiers by customizing size ranges and resolution to your needs with a flexible kit-based solution
- Achieve the highest sensitivity and quantitative performance when sample amounts are limited with LIF detection
- Cover your data management needs through compatibility with the Empower CDS and the Chromeleon CDS

Adapt size ranges and resolving power to your needs



Determine risks of residual DNA in complex viral vector samples

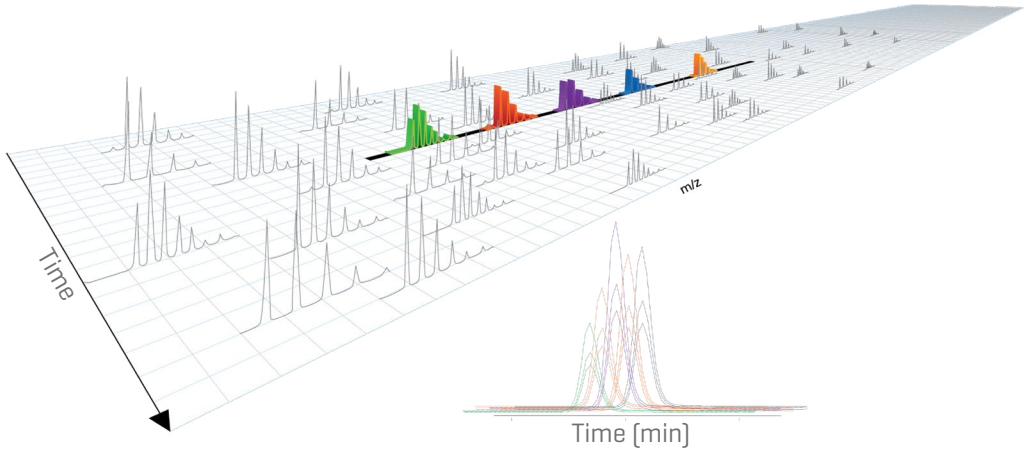


Host cell protein identification and quantitation

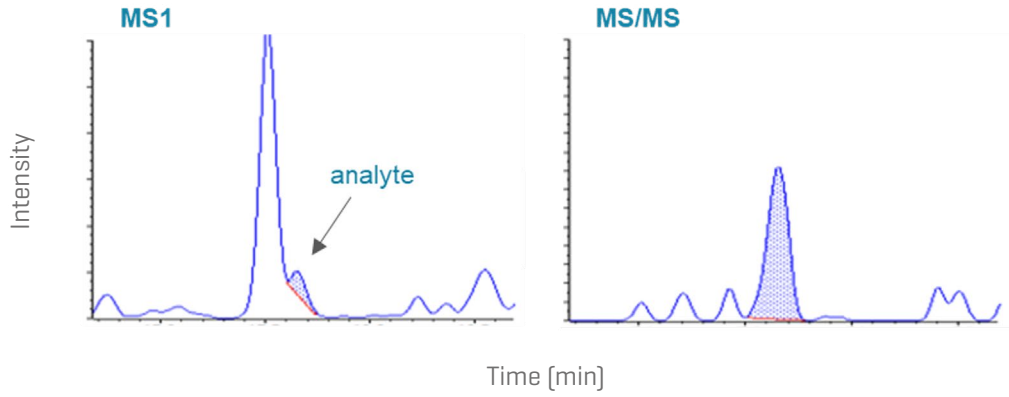
Another class of process-related impurities that can impact the safety and efficacy of viral vector products are proteins derived from packaging cells. The diverse landscape of packaging cell lines and the need to combat future pandemics with unprecedented response times drive the need for new strategies. Identifying process-related impurities with confidence requires highly adaptable workflows that do not need months of development time for different viral vector products.

- Optimize viral process development through relevant information on the identity and quantity of host cell proteins (HCPs)
- Avoid missing critical impurities using an unbiased data-independent acquisition (DIA) approach with **Zeno SWATH DIA**
- Leverage high-quality data from a fast-scanning solution to achieve excellent coverage and detection depth in complex samples despite limited amounts on the **ZenoTOF 7600 system**
- Take back your time for the identification and simultaneous quantitation of residual HCPs without the need for lengthy assay development

Identify impurities with confidence using high-quality DIA



Achieve superior quantitation on the MS/MS level

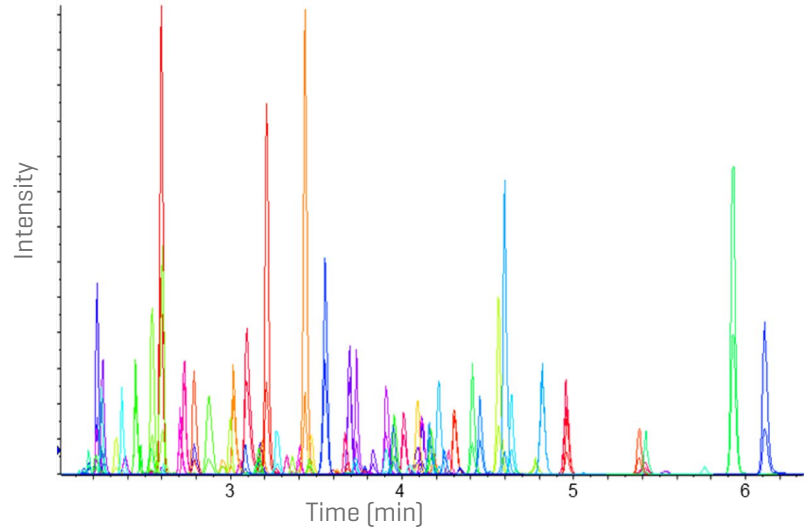


Monitoring of host cell proteins

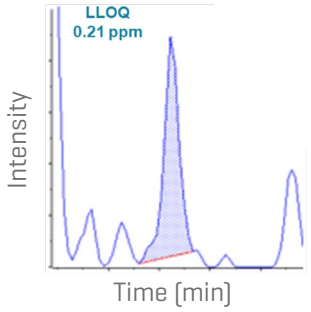
Once problematic HCPs are identified, their tracking throughout development and QC is an important task. Monitoring and quantitation of hundreds of protein impurities can provide information about product quality during process changes, such as upscaling, and reduce risks for the final product. While ligand-binding assays meet quantitation and throughput needs, obtaining actionable results can be a challenge. Understanding which protein impurities have changed can provide tremendous insight that can help streamline optimization of process

- Understand product changes on a protein-specific basis without the need for months of assay development
- Move past bottlenecks and maintain flexibility when packaging cell lines change and no ligand-binding assays are readily available
- Achieve highly sensitive analyte detection, accuracy and precision with the **SCIEX 7500 system**
- Obtain comprehensive results using intuitive data processing with **SCIEX OS software**
- Confidently transfer assays to QC with compliance-ready options and a proven track record of supporting quantitation for GxP environments

Monitor and quantify hundreds of analytes



Rely on a solution with optimal quantitative performance



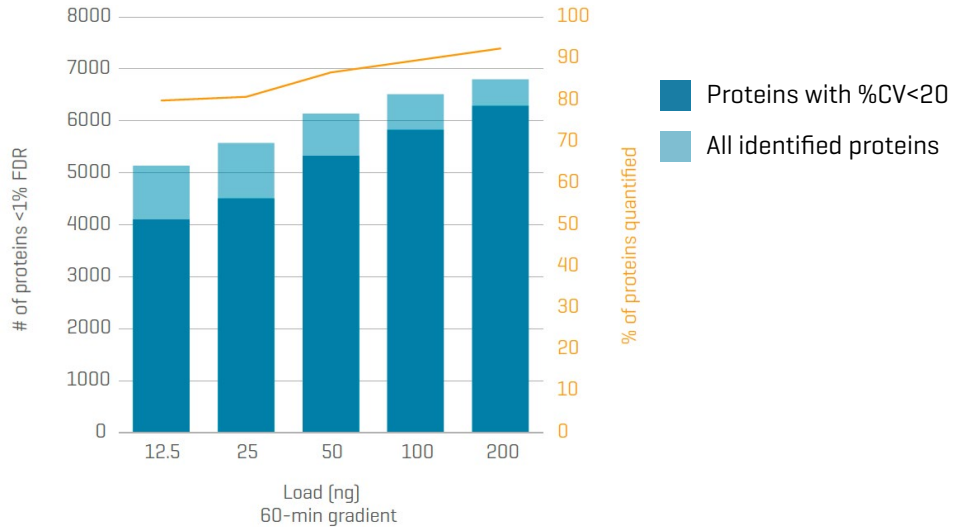
Component Name	Actual Conc...	Num. Values	Percent CV	Accuracy
VNLLSAIK.+2y7.light	0.21	3 of 3	14.89	100.54
VNLLSAIK.+2y7.light	0.85	3 of 3	3.03	97.15
VNLLSAIK.+2y7.light	3.39	3 of 3	11.55	103.07
VNLLSAIK.+2y7.light	13.56	3 of 3	11.84	97.21
VNLLSAIK.+2y7.light	54.23	3 of 3	7.11	106.66
VNLLSAIK.+2y7.light	216.91	3 of 3	6.74	104.26
VNLLSAIK.+2y7.light	867.65	3 of 3	5.06	91.12

Proteome profiling for ex-vivo gene editing

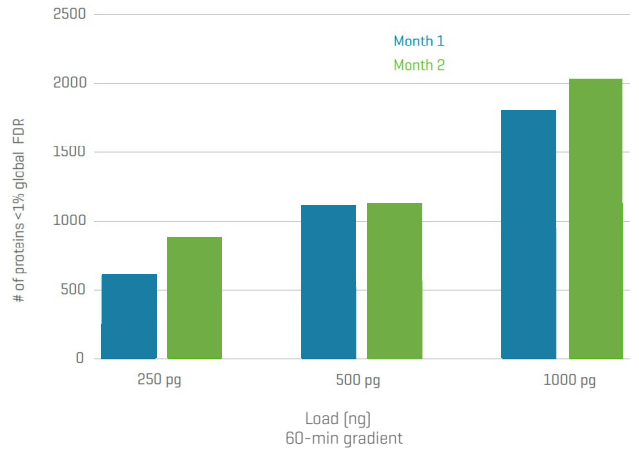
Viral vectors bear the risk of idiosyncratic integration into the host genomes. In addition, gene editing can affect the phenotype in various ways based on the complexity and interdependency of protein networks. Genomic readouts cannot provide sufficient insights into the potential disruption of gene regulators or detect changes to the proteome. Protein assays, such as Western blots, on the other hand, are limited by antibody availability and cannot detect unexpected proteome-wide changes.

- Break through the boundaries of gene editing by seeing and identifying the unexpected
- Understand the effects of gene editing on the proteome level in an unbiased way with DIA using **Zeno SWATH DIA**
- Dig deeper into changes despite limited sample amounts with increased sensitivity using the Zeno trap on the **ZenoTOF 7600 system**
- Achieve confident identification and simultaneous quantitation with excellent MS/MS data quality

Dig deeper into the proteome



Confidently rely on reproducible results despite low amounts



Hardware to provide answers to your questions

ZenoTOF 7600 system

A high-resolution mass spectrometry solution that combines powerful MS/MS sensitivity, fragmentation technology and a step-change in data-independent acquisition

SCIEX 7500 system

The latest generation of triple quads to quantify at lower levels than ever before with impressive precision

BioPhase 8800 system

Built for biopharmaceutical scientists who need the highest data quality and the ability to run multiple samples in parallel

X500B QTOF system

A QTOF system purpose-built to accelerate everyday biologics characterization

PA 800 Plus system

Designed to characterize therapeutic molecules with confidence using high data quality and the kit-based workflows

Software and consumables to meet your needs

Enable highly accurate and informative workflows for full characterization of viral vector proteins with **Biologics Explorer software**

Unleash the analytical power of a next-generation software platform for data acquisition and processing with **SCIEX OS software**

Analyze double-stranded DNA fragments and plasmid isoforms with confidence using the dsDNA 1000 kit

Assess the purity and integrity of RNA therapeutics, vaccines and single-stranded oligonucleotides to help ensure the highest quality with the **RNA 9000 Purity & Integrity kit**

Perform effective quantitation and determination of protein purity and size with the CE-SDS Protein Analysis kit

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SCIEX Now

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- Manage software licenses linked to your registered instruments
- View and report critical instrument statistics when connected to the StatusScope remote monitoring service
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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 learning program that is most suited to your lab and users
- By starting with a clear understanding of your desired learning outcomes, we help you improve lab productivity and consistency by designing and delivering a program that is focused on knowledge advancement and retention

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