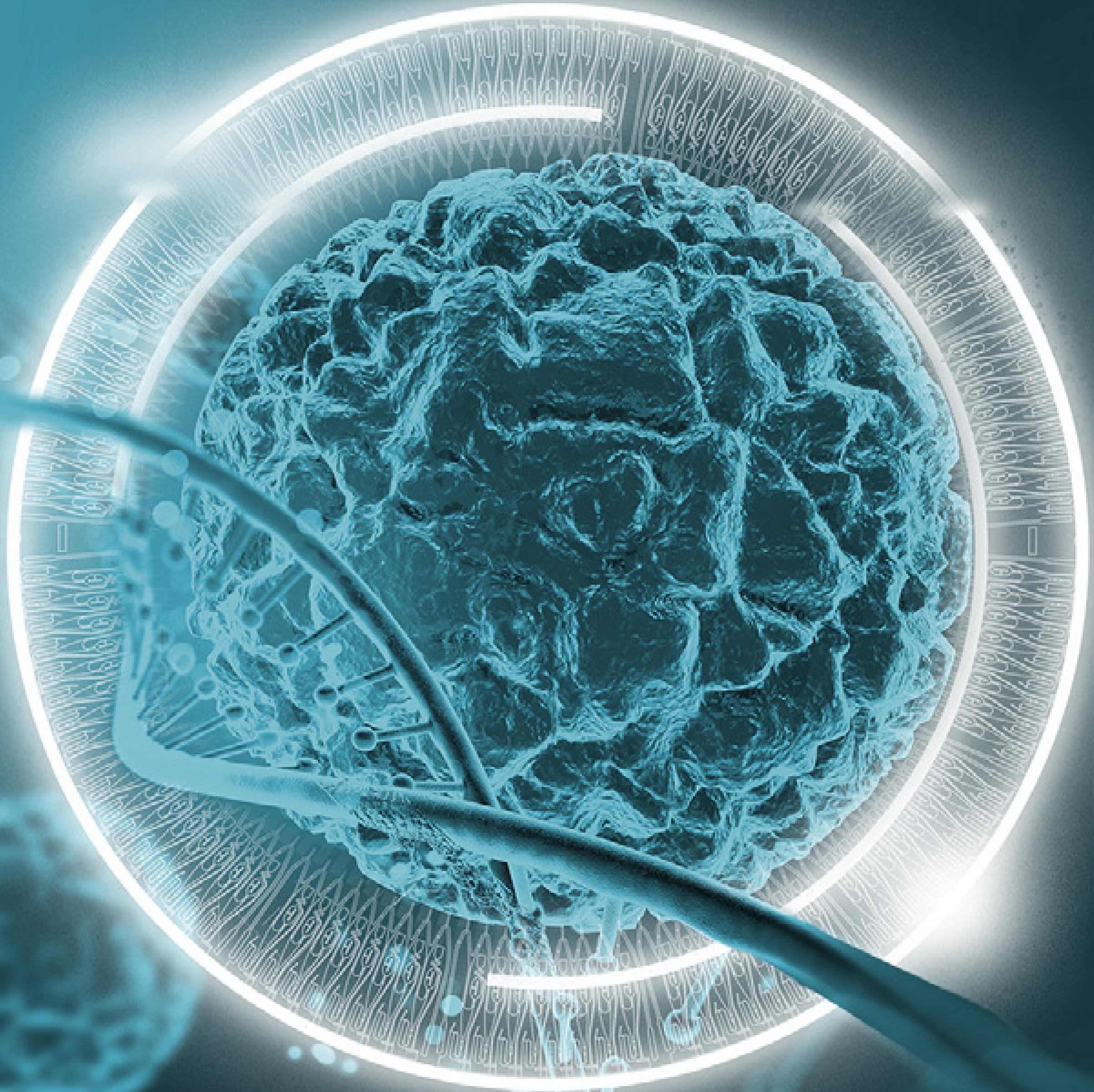
White Paper

Increasing productivity in cell and gene therapy bioprocessing with fast and reliable immunoassays



GYROS PROTEIN Technologies

WHITE PAPER

GYROS PROTEIN Technologies

Increasing productivity in cell and gene therapy bioprocessing with fast and reliable immunoassays

The timely release of safe and efficacious cell and gene therapeutics depends on many factors. One is the availability of immunoassay platforms that can quickly deliver reliable data on viral titer and process-related impurities. There are many factors to consider when choosing an immunoassay platform to ensure high productivity. The system must be robust and quickly generate reliable data from small amounts of precious sample. It should enable rapid method development and still provide flexibility to support the development of novel assays. Automation and a walk-away systems are essential to reducing hands-on-time and minimizing manual errors, enabling personnel to spend time on more important tasks. Added to that, ready validation and a software that enables 21 CFR Part 11 compliance is a must to meet regulatory guidelines. We will investigate the needs of immunoassays in bioprocess analytics for cell and gene therapy in detail and how increased productivity can be met.

The promise of cell and gene therapy

With the first clinical trial conducted in 1990, the start of gene therapy became somewhat of a rollercoaster ride that included initial successes and sobering crashes. The development of much-improved viral vectors has ensured careful and steady progress, with 19 gene therapies approved (including genetically modified cell therapies such as CAR[1] T-cell therapies), 15 RNA therapies approved, and 54 non-genetically modified cell therapies approved as of Q3 2021 (1). The future looks promising, with 3,366 therapies in development as of Q3 2021, ranging from preclinical through pre-registration, and of these 1,890 gene therapies are in development, accounting for 56% of gene, cell, and RNA therapies (1).

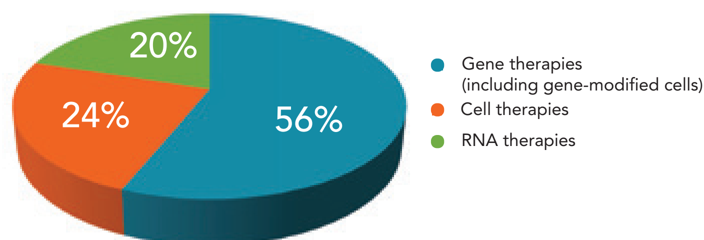
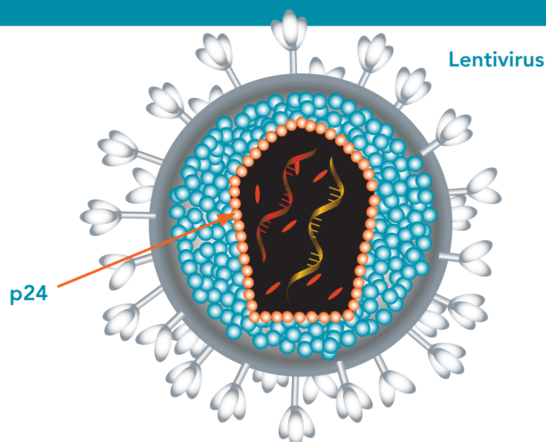
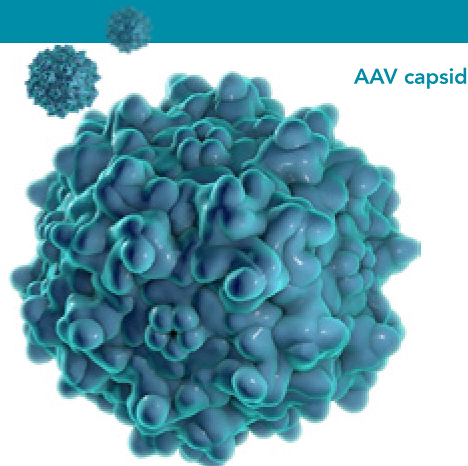


Figure 1. Pipeline therapies by category. Modified from ASGCT/ Pharma Intelligence Quarterly Report Q3 2021 (1)

[1]Chimeric antigen receptor; a complete list of abbreviations can be found at the end of the White Paper.





Adeno-associated viruses and lentiviral vectors for cell and gene therapy

To date, most gene therapies utilize viral vectors, mainly adeno-associated viral (AAV) vectors (and modified AAV) or lentiviral (LV) vectors and to a lesser extent adenovirus, and other viral and non-viral vectors (2, 3). The major difference between LVs and AAVs is genome integration. While LVs integrate their DNA in the host genome, genes delivered by AAVs become an episome, or circular piece of DNA that resides inside the nucleus. Genomic integration prevents the dilution of genetic material over time due to cell division but poses a risk of oncogenesis. Therefore, the nonpathogenic adenovirus-associated virus (AAV) are the most used vectors in *in vivo* gene therapy (2).

AAV vectors are composed of a shell made of proteins that protect the single stranded DNA (transgene). Recombinant AAV can attach to and enter the target cell, transfer to the nucleus, and persist as an episomal form, expressing the transgene in a stable manner. Different AAV serotypes target different organs and tissues (2). For example, AAV2 has a natural tropism towards skeletal muscles, neurons, vascular smooth muscle cells, and hepatocytes and has been used for cancer treatment. AAV8 is a robust vector for gene delivery to liver, skeletal muscle, and heart. The AAV9 serotype can be used to target cardiac and skeletal muscle, liver and pancreatic tissue, the eye, and the central nervous system. The low prevalence of preexisting antibodies to AAV9 in humans also makes this serotype an attractive gene delivery vector (2).

Lentiviral vectors, based on HIV-1 and EIA viruses, are commonly used as vehicles to transfer therapeutic genes (4). Improvements in vector design that increase biosafety and transgene expression have led to the approval of lentiviral vectors for use in clinical studies as well as the commercial approval of new therapies. Lentiviral vectors are often used *ex vivo*, for example in the preparation of CAR T-cells for the treatment of acute lymphoblastic leukemia, but have also been used in direct *in vivo* use.

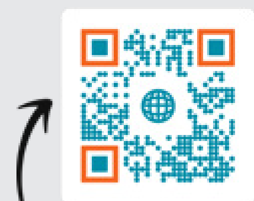
Bioprocess analytics of viral vectors supports process development and quality control

Manufacturing lentiviral and AAV vectors involves cell culture, often based on HEK 293 cell lines. For clinical product manufacturing of viral vectors, the cell culture and purification bioprocess methods implemented should be scalable, and consistently achieve high product safety, purity, potency and stability. The need to determine viral titer (infectious and physical), levels of process-related impurities, and monitor clinical safety risks such as immunogenicity has powered the development of robust analytical methods, including immunoassays. These assays are used to generate high quality data and support efficient method development including the use of tools such as design of experiments (DOE), data-driven decision-making, and release tests for both CMC and final product manufacturing. Since manufacturing batches are often small, immunoassays that support small sample volumes are highly sought after in order to limit consumption of the precious product for analytics.

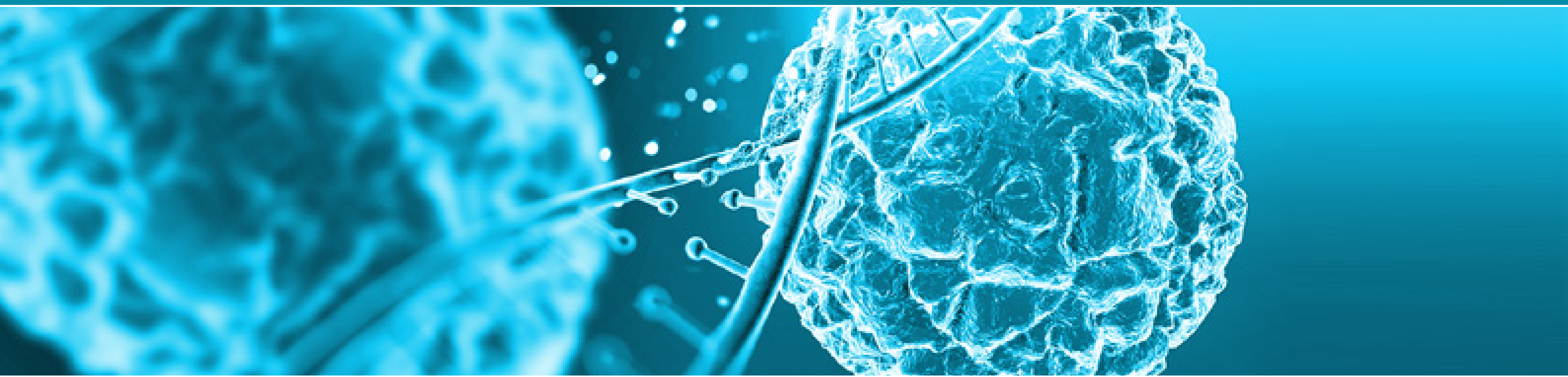
Ready-to-use Gyrolab® Kits and Solutions

A wide range of convenient ready-to-use kits/solutions and assay protocols for use in bioprocess are available:

- Titer (e.g. p24, AAV1-10 and human IgG)
- Host cell protein impurities (e.g. HEK 293, E.coli and CHO)
- Process-related impurities (e.g. EndonucleaseGTP®, Protein A and transferrin)



Scan the QR-code to learn more about our Kits & Solutions



Viral titer determination is a critical quality attribute

Viral titers are either physical titer measured in viral particles, or functional (infectious) titer measured in transduction units. Physical titer is a measurement of how much virus is present and is usually calculated based on the level of a viral protein, such as the lentiviral p24 viral coat protein (4), or viral vector nucleic acids, although these approaches will also measure free molecules that are not associated with a viral particle as well as empty viral particles.

The manufacture of vectors, such as AAV, produces full, partially filled, and empty vectors. The full vectors are the desired product, and the others are considered impurities since they can affect vector efficacy and safety and induce immunogenicity. Additionally, these impurities can inhibit the transduction of full AAVs by competing for vector binding sites on the transfected cells. The ratio between full and empty capsids is therefore a critical quality attribute. Total intact AAV particles can be measured with immunoassays using serotype specific monoclonal antibodies that detect conformational epitopes on assembled AAV capsids. Immunoassays cannot, however, distinguish between empty and full capsid particles. An orthogonal method such as different PCR methods is therefore needed to determine the proportion of capsids with a genome payload and calculate the empty vs full capsid ratio. There are many other methods available to measure AAV titer such as transmission electron microscopy (TEM) or analytical ultracentrifugation (AUC) and each methods has its own advantages and drawbacks.

The functional viral vector titer measures the concentration of viral particles that can transduce cells and can be 100–1000 fold lower than physical titer. Optimizing conditions for viral vector production is slow and laborious and no real-time 'in-line' assay is available. Quantifying functional viral titer is time consuming and costly – the common approach ($TCID_{50}$ assay) can take up to six weeks for an infectivity result, by which time the bioreactor run has been completed. Physical titer is sufficient for most experiments, and functional titer can be calculated from physical titer. As a result, immunoassays are routinely used in process development and release testing.

Impurity testing is key to ensuring safety

Safety has been a key issue in cell and gene therapy. Optimizing downstream purification of viral vectors to meet regulatory requirements includes reducing the level of impurities that can induce toxic or immunogenic reactions in patients, making impurity levels critical to quality. The development of safer non-viral and engineered viral vectors such as modified AAV vectors that are far less likely to elicit immunogenic responses has been a significant step forward.

Impurities can originate from a wide range of sources, such as raw materials in the cell culture media (e.g., growth factors, dithiothreitol and antibiotics), impurities from the consumables and downstream purification process (e.g., ligands leached from chromatography media, endonucleases, or downstream buffer components), or from the cell line used in production (e.g., host cell proteins [HCPs], and host cell DNA). Process-related impurities may present a direct clinical safety risk due to toxicity, immunogenicity, hypersensitivity, endotoxin shock, or the intrinsic biological activity of an impurity. Impurities can also affect the pharmacokinetics of the active substance and therefore efficacy. The main source of concern is, however, the HCPs since these have a complexity and diversity that present a real challenge in terms of both detection and removal.

<u>Host cell proteins</u>

Cell lines such as the human embryonic kidney cell line (HEK 293), adherent or in suspension, are frequently used to manufacture viral vectors used in gene therapy because of their reliable growth and propensity for transfection. HEK 293, for example, contains several adenoviral genes but lacks the key viral replication genes (E1 and E2), which makes the vectors much safer.

Residual HCPs may remain in the purified product, however, and affect product safety, stability, and efficacy. For example, some HCPs are proteases that may degrade the drug substance, while others can be immunogenic, have off-target effects, or reduce the efficacy of the drug. Monitoring the removal of HCPs in drug product during bioprocess development is therefore a regulatory requirement. Finding these HCPs early on in process development can be critical to long-term success in drug development, regulatory submission, and market penetration. Identifying and measuring problematic HCPs, which generally involves

analysis by immunoassays, requires a risk control strategy involving robust downstream bioprocessing to successively reduce HCP levels as much as possible. Specific HCPs that are co-purified with the final viral vector product are then identified using immunoassays based on process-specific reagents.

Process-related additives

Cell culture media can contain components such as transferrin or insulin that can follow the target vector into the purification process. The production of viral vector products can also involve the addition of endonucleases such as Benzonase® or Denarase® during or after host-cell lysis to degrade nucleic acids and disturb macromolecular complexes. Process development and characterization must therefore include determining the amounts of residual additives present throughout the process and the final amounts in the vialed drug product must also be determined as part of QC release testing.

The performance requirements for immunoassays

The prospect of ensuring that a pharmaceutical has the required purity for safe and effective use can be daunting. The key is to adopt a risk-based testing strategy that minimizes the testing effort needed while meeting regulatory requirements and ensuring patient safety. This testing strategy should include analytical methods with several important attributes that ensure the rapid and efficient generation of reliable data:

The need for speed to treat a select few

Cell and gene therapy can offer spectacular successes but also makes very specialized demands on drug development. Treatments are generally only available to a select few, particularly those suffering from genetic disorders previously thought to be incurable. As a result, patient populations are small, with personalized medicine sometimes being refined to truly individualized medicine, making treatments very expensive. Added to that, treatments are often awarded Fast Track designation by the US FDA after Phase I clinical studies for accelerated approval. Long assay times also add to the bottleneck in the development and production of new products (2, 3), emphasizing the need for faster analytical approaches to characterize the therapeutic with regards to quality and titer (4).

The demand for rapid turnaround times means that there is little time to validate new bioanalytical assay technologies, and rapid assay development and sample analysis are critical factors in reducing development times.

Increasing demands on data quality

As the number of clinical studies for AAV and LV-based gene therapies grows, the FDA has emphasized the importance of vector titer assay reproducibility and the measurement of full:empty capsid ratios to facilitate dose comparison between clinical programs. For example, a recent workshop formulated a target of ≤15% precision for measurement of empty AAV capsids for early phase studies, which may require improvements in the reliability of analytical methods for viral vector titer (5, 6).

Getting more data from smaller sample volumes

Vector production is an expensive process that produces small batches of final product. For example, the product of a 200 L bioreactor can be concentrated down to 20 mL. Added to that, regulatory demands have increased the number of analyses required for characterization, putting an even higher premium on analytical techniques requiring less sample. It was estimated by one CMC specialist that almost half of the viral vector production batch may be consumed during QC bioanalysis steps (5), which means that analytical methods that can process very small sample volumes are at a premium.

Considerations when selecting an immunoassay platform for bioprocess analytics

As described above, immunoassay platforms must meet several stringent analytical and workflow-related demands to be an effective tool in cell and gene therapy development and bioprocess analytics. Not only that, the requirements for handling viral vector biosafety must be carefully considered, e.g., the need to minimize sample volumes, and the use of systems that are easily sanitized.

Key factors in choosing an immunoassay platform include:

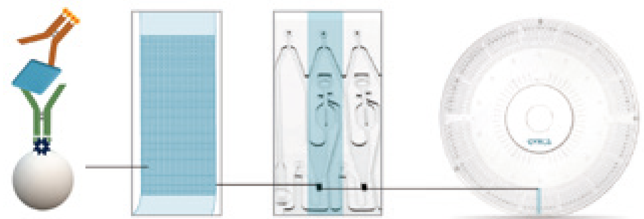
Immunoassay Platform Key Factors	Benefit
High precision and accuracy	Confidence in decisions
Broad analytical range	Reduces need for dilutions and repeats
Robustness	Reliable and repeatable data
Rapid data generation	Meet tough timelines
High throughput	Efficiently handle large sample sizes in development
Flexible open platform	Run multiple assays in parallel to save time Enable the development of novel assays
Automation	Free up scientist's time for other critical tasks and minimize manual errors
Low sample- and reagent consumption	Ensure maximum data generation with the minimum of precious samples and reagents
Readily validated and software enabled for 21 CFR Part 11 compliance	Meet the demands of regulatory guidelines

Miniaturizing immunoassays and maximizing productivity with Gyrolab® platform

The Gyrolab technology meets all these demands by running fully automated nanoliter-scale immunoassays in a Compact Disk (CD) format, with low sample and reagent consumption, all with exceptional reproducibility. Gyrolab systems are well established in the pharmaceutical industry, including preclinical and clinical contract research organizations (CROs) and contract manufacturing organizations (CMOs). They support a wide range of applications used throughout cell and gene therapy development including AAV immunogenicity assessment, viral vector titer determination, and the analysis of process impurities such as HCPs, leached ligands, and additives. The examples below illustrate the benefits of using Gyrolab systems in some of the most important applications in bioprocess analytics for cell and gene therapy. A wide range of ready-to-use kits and solutions for bioprocess analytics of viral vectors using the Gyrolab technology are available to meet the demands for assay performance and speed required to succeed in cell and gene therapy development.

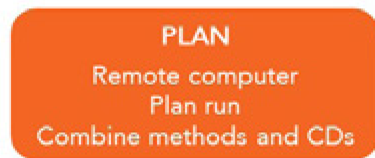
Gyrolab systems

The Gyrolab systems perform automated immunassays within nanaoliter-scale microfluidic structure in a Compact Disk (CD) format. Each structure on the CD comprises a 15 nL affinity column pre-packed with streptavidin-coated particles, dramatically reducing the sample and reagent volumes as compared to plate-based ELISAs.



Gyrolab xPand *can hold up to 5 CDs, which enables different methods and CDs to be mixed and matched to meet specific needs. The control and analysis software enables 21 CFR 11 compliance which enables assay transfer from development through to GMP environments*

Gyrolab xPlore™ *is a single-CD, cost-effective platform that makes automated nanoliter-scale immunoassays readily accessible to any bioanalytical laboratory.*



Gyrolab Systems

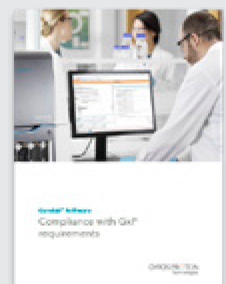
Immunoassays the way you´ve always wanted

DOWNLOAD

Gyrolab Software

Compliance with GxP requirements

DOWNLOAD



Gyrolab applications in cell and gene therapy

Here we present some examples of the many ways Gyrolab immunoassays can boost productivity in bioprocess analytics to support cell and gene therapy. These examples are based on data produced by both external collaborators and in-house investigations.

Viral titer determination

AAV vectors

The automated Gyrolab system generates 96 data points per CD, within 70 minutes. The data is comparable to ELISA, which builds confidence in a transition from the traditional immunoassay method. Figures 2 and 4 show standard curves for various AAV serotypes using the ready-to-use Gyrolab AAV9 Titer Kit and Gyrolab AAVX Titer Kit, respectively. Figure 2 compares the Gyrolab AAV9 titer assay with manual traditional ELISA and demonstrates the broader dynamic range of Gyrolab assays. This reduces the need for dilutions and repeat analysis. The excellent dilutional linearity, as shown in Figure 4, ensures that accurate results can be obtained from the range of diverse samples involved in bioprocess analytics. Figure 3 presents titer data from a contract research lab of samples taken from various stages of a AAV9 process run and assessed using Gyrolab versus manual ELISA. Again the comparability with ELISA is demonstrated across all matrices from upstream processing (USP) to downstream purification (DSP).

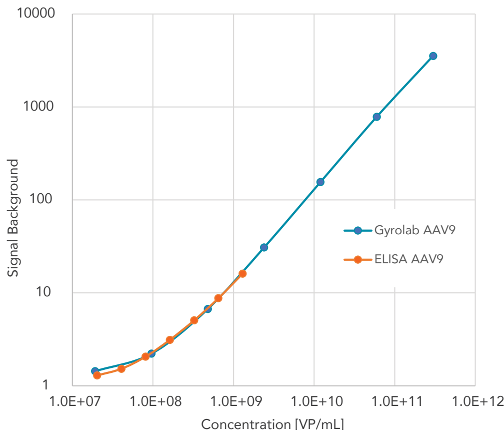


Figure 2. Gyrolab AAV9 Titer Kit generates data comparable to ELISA and extends the analytical range by over 2 logs.

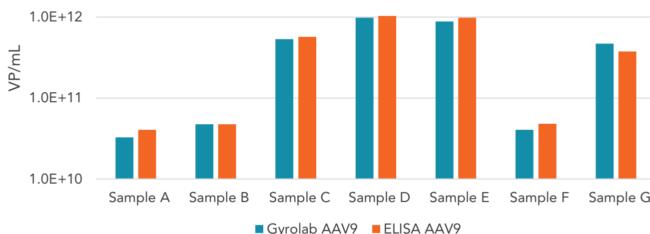


Figure 3. Gyrolab AAV9 Titer Kit and a manual capsid ELISA gave comparable results for a range of samples.

Courtesy of CRO partner providing analytical services for cell and gene therapy customers.

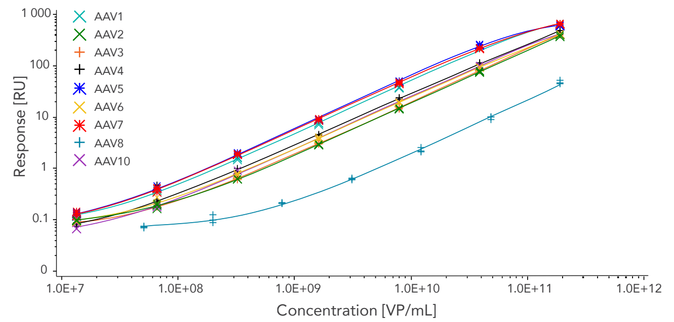


Figure 4. The multi-serotype detection Gyrolab AAVX Titer Kit in combination with the Gyrolab system quickly delivers high quality titer data for AAV serotypes 1–8 and AAVrh10.

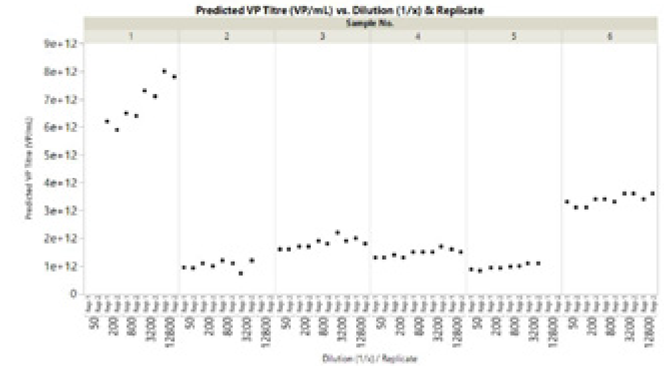


Figure 5. Gyrolab AAVX Titer Kit shows good dilutional linearity with comparable predictions for viral particle titer whether the sample was diluted 1:50 or 1:12800. Data is for serotype AAV5.

Courtesy of partner in clinical-stage gene therapy company.

Lentivirus titer

The combination of Gyrolab assays and the automation of the Gyrolab system delivers high precision data to build confidence in data driven decision making. The need for high precision when quantifying AAV titer, for example was noted in an interview with Christine Le Bec, Head of CMC Gene Therapy at Sensorion Pharma, in Cell & Gene Therapy Insights (6). The Food and Drug Administration (FDA) now requires very low variability with not more than 15% target for precision, which helps them make easier comparison between different labs and clinical trials (6, 7).

The Gyrolab p24 Titer Kit, used for determining LV titer, generates data with high precision (<6% CV over 6 runs) as shown in Figure 5, meeting high precision requirements (7).

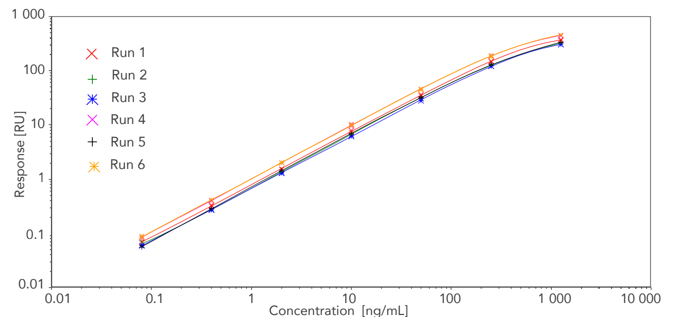


Figure 6. The Gyrolab p24 Titer Kit generates data with high precision. This is an overlay plot of standard curves from six runs on four instruments. Intra- and inter-run variation was less than 6% CV for all standards.

Analysis of process-related impurities

Host cell proteins

HCPs are commonly analyzed by ELISA, but this method can be laborious and consume large amounts of precious sample and reagents. This has driven the evaluation of alternative platforms, such as the Gyrolab system, to boost productivity. The generation of comparable data using ELISA and a Gyrolab assay builds confidence in this transition.

Figure 7 presents HCP data from Viralgen Vector Core, an AAV contract manufacturing lab that assessed HEK 293 HCP impurities in samples from different process steps using the HEK 293 HCP Solution for Gyrolab, with the HEK 293 Assay Reagent Set for Gyrolab from Cygnus Technologies as compared to manual ELISA using the comparable ELISA HEK 293 HCP kit from Cygnus. Values were similar between the Gyrolab system and manual ELISA, although Gyrolab provided higher through-put, supported a wider dynamic range (3 log) and generated reproducible data from smaller sample volume (only 8 µL/sample). Excellent sensitivity (<4 ng/mL), broader sample dilutional linearity and good spike recovery were also obtained (results not shown).

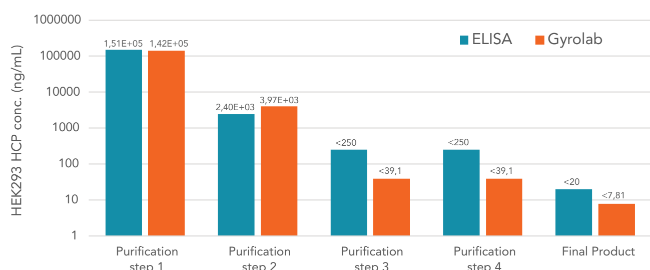


Figure 7. Gyrolab HEK 293 HCP Solution and traditional ELISA were used to measure the concentrations of HEK 293 HCPs in samples from different stages in the purification of an AAV vector. The two assays gave comparable data for HCP levels. Values below the LOQ are marked with '<'. The data was supplied by Viralgen Vector Core, a CDMO engaged in gene therapy manufacturing.

Endonuclease

A clinical-stage gene therapy company was faced with the challenge of designing an assay to detect residual endonuclease for in-process and final rAAV drug product samples with increased throughput and improved analysis as compared to a commercially available ELISA kit. EndonucleaseGTP® Solution for Gyrolab with the EndonucleaseGTP Assay Reagent Set for Gyrolab from Cygnus Technologies was used in combination with EndonucleaseGTP Antigen Concentrate (Cygnus Technologies) as the standard. This combination proved to be an effective alternative to the commercially available ELISA kit previously used and exceeded the acceptance requirements, which was set as any improvements over the ELISA results. As seen in Table 1, Gyrolab provided faster analysis, lower sample volume, higher productivity and broader dynamic range.

Table 1. Performance data from manual ELISA and results of evaluation of Gyrolab assay for endonuclease determination. Acceptance criteria was set to any improvements over ELISA results.

	ELISA	GYROLAB
TURNAROUND TIME	4 hours	~2 hours
SAMPLE VOLUME REQUIRED	100 µL	~8 µL
LIMIT OF DETECTION	200 pg/mL	50 pg/mL
SAMPLES PER RUN	18 samples	36 samples
LINEAR RANGE	5 ng/mL – 0.2 ng/mL	40 – 0.05 ng/mL

Transferrin and insulin

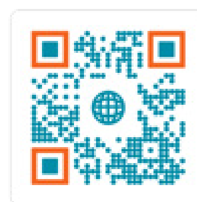
Gyrolab systems are supported by an increasing range of ready-to-use kits, and yet remain as open systems that enable the in-house development and evaluation of high-performance custom immunoassays. Gyrolab assay protocols are also available to accelerate the development of bioprocess analytics. Two examples are Gyrolab Assay Protocols for transferrin and insulin, which are cell culture media impurities that need to be reduced to a minimum during downstream purification.

Rapid parallel analysis of CQAs using a Gyroplex® panel

Vector production is an expensive process that results in a small volume of highly valuable therapeutic product. Bioprocess analytics that include the determination of capsid particle titer and impurity levels must therefore be efficient and consume minimal volumes of sample.

The Gyrolab xPand system has room for 5 CDs and can therefore run at least 5 different single plex assays (a Gyroplex panel) in one single automated run.

Table 2 and 3 show the set-up and results from a Gyroplex panel simulating samples taken from various steps in a downstream process of two separate AAV serotypes batches (AAV2 and AAV9). Total capsid titer for AAV2 and AAV9 and three process-related impurities assays (HEK 293 HCP, EndonulceaseGTP and transferrin) were run on Gyrolab xPand, generating 480 data points in less than 6 hours. The assays used up less than 50 µL of sample in total and required only approximately 1 hour hands-on time to set up the assays and start the run. This approach enabled a full assessment of production batches of different viral vectors to be made within a working day and with minimum effort and maximal output.



Scan the QR-code to learn more about Gyrolab Kits & Solutions

Table 2. Assays used in Gyroplex panels to analyze samples from AAV2 and AAV9 vector production.

Analyte	Kit/Assay	Gyrolab Bioaffy™ CD	Approximate analytical range	
			LLOQ	ULOQ
AAV2	AAVX Titer Kit	1000	1.0E8 VP/mL	1.0E11 VP/mL
AAV9	AAV9 Titer Kit	1000	2.0E8 VP/mL	2.0E11 VP/mL
HEK 293 HCP	HEK 293 HCP Solution for Gyrolab	1000 HC	4 ng/mL	8000 ng/mL
Transferrin (human)	Gyrolab assay protocol for transferrin	1000	0.1 ng/mL	150 ng/mL
Endonuclease	EndonucleaseGTP Solution for Gyrolab	1000 HC	0.05 ng/mL	200 ng/mL

Tables 3. Summary of results for Gyroplex of AAV2 (a), and AAV9 (b), showing titers and process-related impurity determinations of HEK 293 HCPs, endonuclease, and transferrin. Assay acceptance criteria for all impurity determinations were 20% deviance from highest valid dilution and at least 3 valid dilutions in the dilution series accepted. Data produced in-house.

Sample ID	AAV2		HEK 293 HCP		Endonuclease		Transferrin	
	Average conc. (VP/mL)	CV series conc. (%)	Average conc. (ng/mL)	CV series conc. (%)	Average conc. (ng/mL)	CV series conc. (%)	Average conc. (ng/mL)	CV series conc. (%)
1	8.93E+08	6.6	4531	4.8	199	1.6	197	2.7
2	3.84E+09	2.5	674	3.6	24.4	1.6	20.9	1.2
3	1.96E+10	1.2	171	2.4	4.74	10.0	2.01	0.8
4	1.95E+11	5.8	48.0	8.1	0.94	7.6	0.47	11.5
5	1.54E+09	3.0	4369	5.9	195	3.7	193	3.2
6	6.61E+09	4.3	674	3.7	23.4	2.9	20.3	5.8
7	3.51E+10	4.3	159	2.2	4.46	3.9	1.93	8.7
8	3.70E+11	2.9	35.7	9.3	0.87	1.9	0.43	1.2

Conclusions

The development and manufacture of products for cell and gene therapy place a lot of pressure on bioprocess analytics to deliver reliable data quickly and efficiently from small sample volumes. Immunoassays such as ELISA are frequently used to measure critical quality attributes such as virus titer and impurity levels but can be laborious and consume large amounts of precious sample. Gyrolab systems offer a powerful automated alternative that can generate data comparable to ELISA but with less hands-on time, lower consumption of precious sample and reagents. They also provide higher precision, and a broader dynamic range that reduces the need for re-analysis. Added to that, the availability of ready-to-use kits and solutions for assessing titer (AAV 1-10 and lentivirus p24) as well as the most common host cell protein and process impurities reduces the time needed for method development and validation. The Gyrolab software supports 21 CFR Part 11 and the system is thereby compliant to be used in a regulated environment such as QC labs. As a result, the Gyrolab platform is penetrating the cell and gene therapy market at a rapid pace as many biopharmaceutical labs, including preclinical and clinical CROs and CDMOs, are experiencing increased productivity when implementing the Gyrolab technology in their bioprocess analytical workflows.

References

1. ASGCT/Pharma Intelligence Quarterly Report Q3 2021.
2. Rininger J, et al. Capacity analysis for viral vector manufacturing. Is there enough? BioProcess Int. 2019; 17(11).
3. Transfiguracion J, et al. Rapid in-process monitoring of lentiviral vector particles by high-performance liquid chromatography. Mol. Ther. Meth. Clin. Dev. 2020; 18: 803–10.
4. Gene Therapies Push Viral Vector Production – Bioprocess Development Forum.
5. Priorities for AAV vector analytics development. Interview with Christine Le Bec. Cell & Gene Therapy Insights 2020; 6(7), 871–875
6. Quantitation of AAV-based gene therapy products – 12/07/2018. FDA.

List of abbreviations

CAR, chimeric antigen receptor; AAV, adenovirus-associated virus; HIV, human immunodeficiency virus; EIA, equine infectious anemia; HEK, human embryonic kidney; CQA, critical quality attribute; CMC, chemistry, manufacturing and control; qPCR, quantitative polymerase chain reaction; TCID50, median tissue culture infectious dose; HCP; host cell protein; ELISA, enzyme-linked immunosorbent assay; CV, coefficient of variation; VP, virus particle; LLOQ, lower limit of quantitation; ULOQ, upper limit of quantitation; LOD, limit of detection; CV, coefficient of variation; TE, total error, FDA, Food and Drug Administration; CDMO; contract development and manufacturing organization; CRO, contract research organziation

Gyrolab, Gyroplex and Rexxip are registered trademarks and Gyros, Gyrolab xPlore, Bioaffy and Gyros logo are trademarks of Gyros Protein Technologies Group. All other trademarks are the property of their respective owners. Products and technologies from Gyros Protein Technologies are covered by one or more patents and/or proprietary intellectual property rights. All infringements are prohibited and will be prosecuted. Please contact Gyros Protein Technologies AB for further details. Products are for research use only. Not for use in diagnostic procedures. © Gyros Protein Technologies AB 2022.