ThermoFisher SCIENTIFIC

GENE THERAPY
FROM SET-UP TO SCALE-UP

We connect you to flexible, scalable solutions in support of swift and safe development of your gene therapies.

CONTENTS

Collaborate

Our team of scientists, process development professionals and regulatory specialists, provides the guidance to help you achieve commercial success, including lab setup, product selection, process development, documentation, and more.

Accelerate

With integrated end-to-end solutions and products designed with your endpoint in mind, we can help accelerate your timelines from discovery to commercial manufacturing.

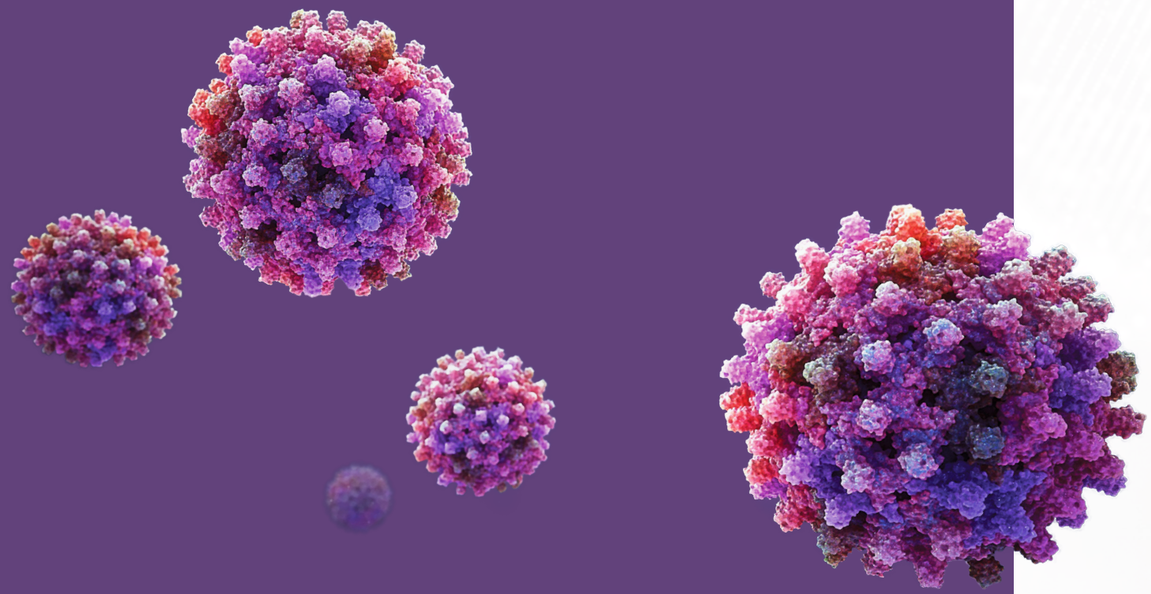
Flexibility

Our advanced infrastructure, trained experts, and state-of-the-art technologies provide the ability to seamlessly blend our products and services to fit your business needs. Whether you are manufacturing in-house or outsourcing, connect to a partner who can flex with you.

OVERVIEW

The goal of gene therapy is to create a treatment with the potential to save or transform lives by modifying a defective gene or replacing it with a more functional one. Producing safe, effective, and reproducible gene therapies can be more complicated than meets the eye. Success within this complex space requires a partner with knowledge and connections to help you overcome obstacles and accelerate your research and therapeutic production.

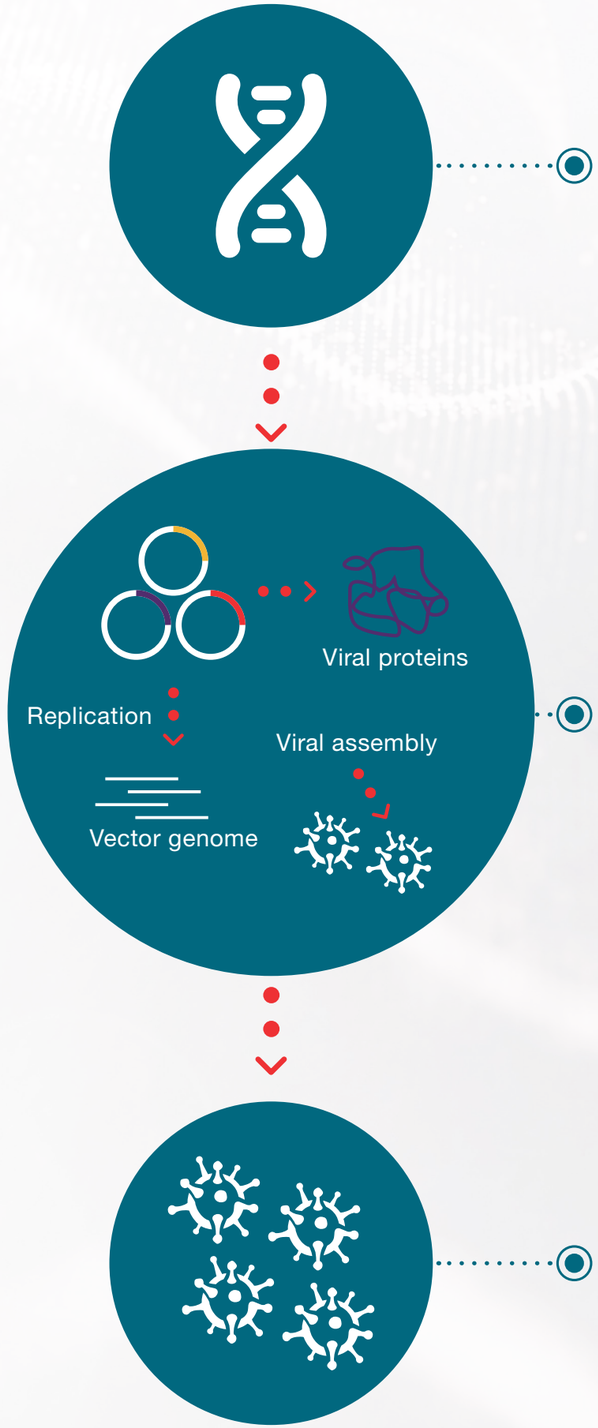
No matter in what stage of research, development, or manufacturing you are, our dedicated experts will connect you with cutting-edge scalable solutions to meet your unique specifications. Whether you are developing in-house capabilities or outsourcing your projects, we will work with you as your reliable, full-service partner at every phase.



VIRAL VECTOR PLATFORMS FOR GENE THERAPY

Gene therapy involves delivery of a functional gene or transgene to a target cell. A common approach to achieve this is by using a viral vector. Viral vectors have high cellular uptake and advancements in viral vector design have significantly reduced immunogenicity.[1]

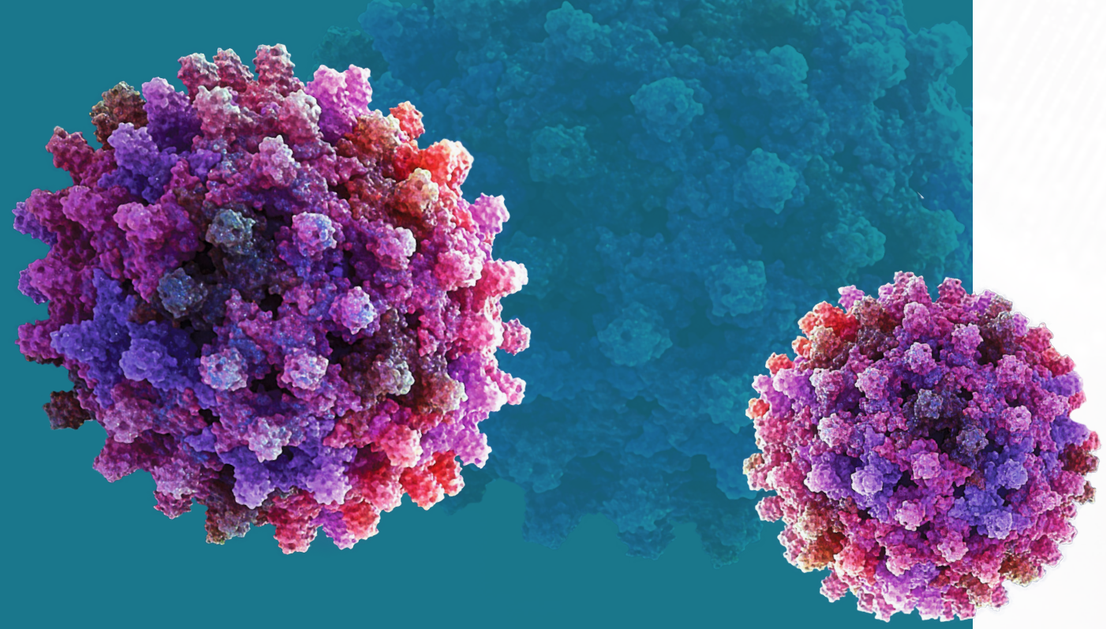
The two most common viral vectors, adeno-associated virus (AAV) and lentivirus (LV), have distinct characteristics that lend themselves to specific applications. Lentiviral vectors can accommodate relatively large target genes, and integrate into the genome of their host target cells, making them suitable for gene therapies targeting dividing cell types. In contrast, AAV vectors are useful for the delivery of smaller genes, and are non-integrating.



Plasmid DNA containing the transgene and packaging plasmids are complexed with a transfection reagent

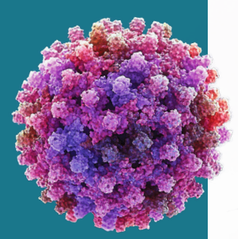
Viral production cell line is transfected with the DNA/ transfection reagent complex

Following incubation, viral particles are harvested.



VIRAL VECTOR PRODUCTION FOR USE IN GENE THERAPIES ENCOMPASSES MULTIPLE STEPS

Intended use of the products mentioned in this brochure vary. For specific intended use statements, please refer to the individual product label.



Plasmid construction

Gene synthesis

Cloning and assembly

Large-scale plasmid purification

Vector production

Gene delivery

Virus-producing adherent and suspension cells

Custom media

current Good Manufacturing Practices (cGMP) chemicals and process liquids

Specialized laboratory equipment

Vector purification

Affinity chromatography

Ion exchange chromatography

Centrifugation

Process liquid/buffer preparation services

Lot release and characterization

Identity, purity, and contamination

Functional titer

Empty capsid analysis

Genomic, proteomic, and cellular analysis tools

Formulation, supply chain and logistics

Aseptic fill and finish

Cryopreservation

Cold chain supply logistics

Clinical trial support

Global distribution

VECTOR CONSTRUCTION

Production of a quality viral vector starts from plasmids encoding the gene of interest and viral packaging genes.

Step 1: Prepare bacterial media

Key products

Gibco™ Bacto™ CD Supreme Fermentation Production Medium

Key benefits

- Reduce lot-to-lot performance variability with a 100% chemically defined formulation
- Eliminate risk of bacteriophage and BSE/TSE contamination*
- Optimize your fermentation workflow by streamlining, reducing, or eliminating steps
- Increase growth and production yields
- Flexible sterilization methods allow the medium to be filter-sterilized or autoclaved
- Scalable format to meet your development needs

Step 2: Grow bacteria containing your plasmid of interest

Key products

Thermo Scientific™ HyPerforma™ Single-Use Fermentor (S.U.F.)

Key benefits

- Maintain sterility throughout the fermentation process
- High oxygen transfer with minimal liquid loss
- Powerful mixing for high mass transfer
- Increased cooling capability
- Automated foam controls

Step 3: Purify plasmid

Key products

Chromatography columns

- Thermo Scientific™ POROS™ AEX Resins: XQ, HQ50, D50, PI50
- Thermo Scientific™ POROS™ Hydrophobic Interaction Chromatography (HIC) Resins (Ethyl, Benzyl, Benzyl Ultra)

Key benefits

- Excellent purification of larger molecules due to unique bead pore structure
- High resolution for efficient separation
- Effective systems reduce the number of purification steps to help save time, money, and preserving yield

Step 4: Assess for process impurities

Key products

Applied Biosystems™ resDNASEQ™ Quantitative DNA Kits

Key benefits

- Fully integrated real-time PCR system for quantitation of residual DNA
- From in-process samples with different sample matrices to purified final product, you can ensure a high degree of confidence in quantitative data obtained from a wide range of sample types.

*This product does not contain any raw materials of direct animal origin or materials that have been produced using animal-origin components. It has not been in contact with material of animal origin during processing and therefore poses no TSE risk.

A complete line of equipment is available to support your plasmid production needs, from discovery through scale-up and production.

Incubated orbital shakers

For small-scale growth of transformed bacteria. Accurately maintains temperature and speed for high reproducibility.

See the complete line at **thermofisher.com/shakers**

Biological safety cabinets

Feature SmartFlow technology, Digital Airflow Verification (DAVe) with alarm signals to maintain safety within your laboratory.

See the complete line at **thermofisher.com/bsc**

Microbiological incubators

Available in a wide variety of sizes for different scales and applications.

See the complete line at **thermofisher.com/incubators**

Centrifuges

Reliable centrifuges accommodate a broad range of sample sizes, up to 8 x 2 L bottles.

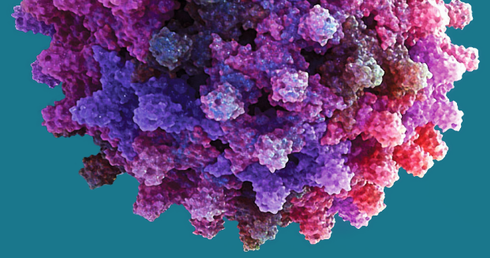
See the complete line at **thermofisher.com/centrifuges**

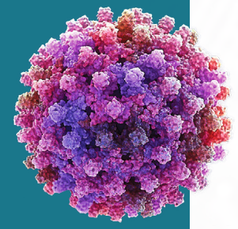
NanoDrop instrument

Quickly determine your plasmid DNA concentration using a Thermo Scientific™ NanoDrop™ instrument.

See the complete line at **thermofisher.com/nanodrop**

Looking for cloning products to support discovery? See our complete line of cloning products at thermofisher.com/cloning





VECTOR PRODUCTION

Cost-effective LV and AAV vector production is critical to meet commercial demand, and a smooth ramp-up to clinical production is essential. Thermo Fisher Scientific offers a range of scalable products:

Complete production system solutions

- Gibco™ AAV-MAX Transfection Kit
- Gibco™ LV-MAX™ Lentiviral Production System

Custom production solutions for AAV

- Gibco™ Viral Vector HEK Media Panel
- Custom manufacturing of internally developed formulations
- Rapid prototyping of media
- Manufacturing of customer-owned formulations

Cell culture vessels

- Thermo Scientific™ Nalgene™ shaker flasks

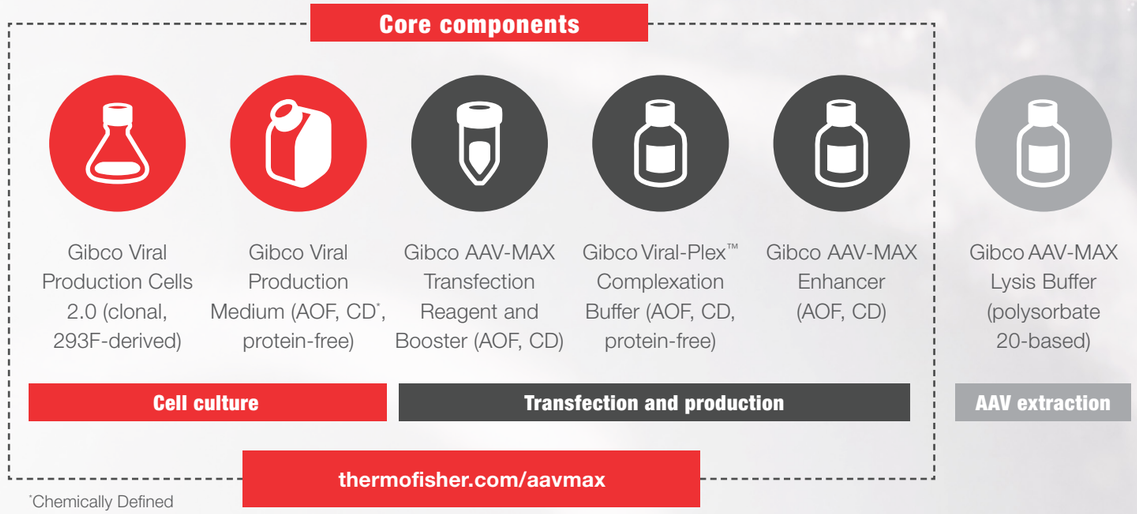
Production of AAV with AAV-MAX Helper-Free AAV Production System

The Gibco™ AAV-MAX Helper-Free AAV Production System is a complete suite of components designed and optimized to produce adeno-associated viral vectors using a HEK293 suspension cell system. This complete solution is a cost-effective, scalable system designed to transition your workflow from discovery to commercial manufacturing.

The AAV-MAX system features:

- **High AAV titers—≥ 5 x 10^{10} vg/mL (unpurified)**—more viral particles per volume of production to help reduce production costs
- **Scalability**—suspension system with scalable protocols, from shaker flask to bioreactor scale
- **Simplified workflow**—streamlined protocol using helper virus-free triple transfection
- **Animal origin–free (AOF)**—no animal- or human-derived components to reduce safety risk of raw materials
- **Clonal 293F-derived producer cells**—high-producer clonal cell line; documented, cGMP bank**

**cGMP bank will be available with the Gibco™ Cell Therapy Systems™ (CTS™) AAV-MAX Production System



*Chemically Defined

Production of LV with CTS LV-MAX Lentiviral Production System

The Gibco™ CTS™ LV-MAX™ Lentiviral Production System is a complete, xeno-free, optimized, scalable, and integrated solution for production of lentiviral vectors in a suspension cell platform. The system can produce titers greater than 1 x 10^8 TU/mL (unconcentrated), resulting in cost savings of up to 50% compared to polyethylenimine (PEI)–based lentiviral production methods.

The CTS LV-MAX system is manufactured in conformity with GMP for medical devices (21 CFR Part 820) and follows USP <1043> and European Pharmacopoeia (Ph Eur) 5.2.12 recommendations. All CTS products come with a Drug Master File or a Regulatory Support File.

cGMP-banked suspension HEK293 cell banks for viral vector production

Cell lines have been developed to support viral vector production for cell and gene therapy applications. These cells have been adapted for suspension culture to facilitate scale-up. For more information on these cell lines, please contact outlicensing@thermofisher.com. Fully documented cGMP-banked cell line (HEK293F-derived) with detailed historical cell lineage file.

The ExpiSf system, a chemically defined baculovirus–insect cell expression system for AAV production

The Gibco™ ExpiSf™ Expression System (Sf9) is an insect cell–based production system that can be used for AAV production. Like the LV-MAX and AAV-MAX systems, the ExpiSf Expression System is a complete optimized system. To learn more about the use of the ExpiSf system for the production of AAV, see our application note.

Learn more about the Gibco LV-MAX Lentiviral Production System at **thermofisher.com/lvmax**

Gibco™ Viral Vector HEK Media Panel

The Gibco™ Viral Vector HEK Media Panel provides a diverse offering to accelerate gene therapy development and production. Covering a broad variety of HEK293 cell types and not tied to specific transfection reagents or techniques, the ready-to-use formulations will help you identify an optimal formulation for target cell lines.

Features:

- Designed to be compatible within your workflow
- Support from dedicated scientists to help determine the best path forward
- Customizable and available in Gibco™ Advanced Granulation Technology™ (AGT™) formulations

Benefits:

- Simplicity: Ready-to-use RUO formulations
- Diversity: Distinct formulations to match each cell lineage's nutritional requirements
- Productivity: Improved titers over industry standard

Learn more about the Viral Vector HEK Media Panel at **thermofisher.com/hekpanel**

SETTING UP YOUR OWN VIRAL PRODUCTION PLATFORM?

We offer catalog and custom media solutions for producer cell culture and viral vector production

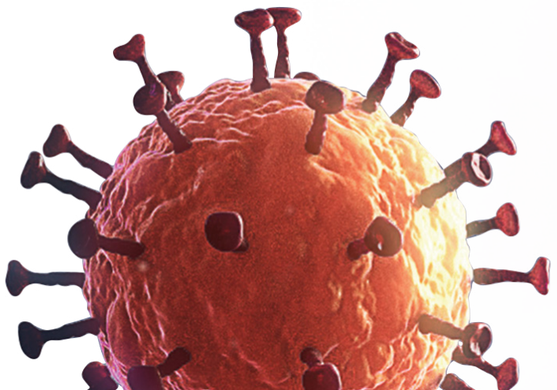
Gibco™ media is manufactured in compliance with cGMPs, a robust quality management system, and decades of experience.

Gibco products come in an array of configurations and formats to suit your particular application. From the cutting-edge Gibco™ Advanced Granulation Technology™ (AGT™) format to large-scale bioprocessing liquids, we can help you find the best format, size, and packaging to meet your needs. Customization options are available for both media formats (liquid and powder), with a focus on flexibility and performance.

When standard packaging does not meet your needs, our expert packaging engineers are ready to help create a custom solution for you.

Our strict control over sourcing raw materials, enabled by deep analytical expertise, helps reduce your risk in media manufacturing.

Learn more today

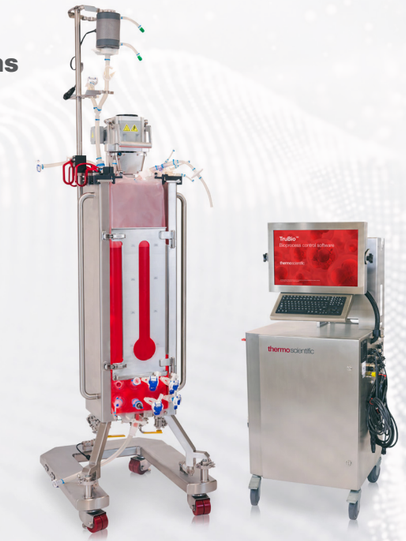


QC testing performed on all cGMP media products to support your needs

- **pH**
- **Osmolality**
- **Sterility**
- **Stability**
- **Mycoplasma testing**
- **Virus testing**
- **Amino acid analysis**
- **Custom testing solutions**

Growth vessels

Scale-up to meet your production demands with a wide range of products to fit your needs at various stages of production. From plates and flasks used in discovery through automated, integrated 2,000 L bioreactors, our growth vessels and equipment are designed to meet the rigorous demands of commercial-scale viral production at every step.



The HyPerforma DynaDrive Single-Use Bioreactor (S.U.B.) and G3Lite Bioprocess Controller with TruBio automation software

HyPerforma DynaDrive Single-Use Bioreactor (S.U.B.) and G3Lite Bioprocess Controller with TruBio automation software

An open architecture control system that can be integrated with any single-use bioreactor, such as the Thermo Scientific™ HyPerforma™ DynaDrive™ Single-Use Bioreactor (S.U.B.) system (available in sizes ranging from 50–5,000 L). The system consists of a control tower that leverages intelligent transmitters, mass flow controllers (MFCs), pumps, sensors, and Thermo Scientific™ TruBio™ bioprocess automation software that facilitates easy, reliable, and repeatable process development and commercial cell culture processes. Thermo Scientific™ HyPerforma™ G3Lite™ Bioprocess Controllers are fully self-contained, movable units that can be operated as stand-alone or networked for multiple vessels, for use in non-GMP- and cGMP-certified production facilities.

Learn more at **thermofisher.com/dynadrive**

Scale your cultures and experiments with confidence

Thermo Fisher Scientific offers solutions to seamlessly scale up your production while maintaining sterility, pH, and stability. These include catalog, configurable, and custom solutions that optimize the chemicals, packaging, and format to reduce waste and improve productivity. Customized fluid transfer solutions can save sterility costs and reduce the risk of operator-induced variation.

Thermo Scientific™ Harveststainer™ BioProcess Container (BPC)

Help ensure full containment of your cell culture supernatant in a closed, single-use system. The Harvestainer BPC is designed to retain ≥90 µm diameter microcarriers while allowing the supernatant to pass through the next process stage.
Learn more at **thermofisher.com/harvestainer**

Thermo Scientific™ Labtainer™ Pro BPC with BioTitan™ Retention Device

Your single-use, closed system with an optimized user experience (available in nine sizes, ranging from 50 mL to 20 L).
Learn more at **thermofisher.com/labtainerpro**

Thermo Scientific™ Nunc™ Standard Closed Cell Factory™ system

Having a clean and closed system that provides consistent and high-quality results should be a standard among your adherent cell culture processes. The closed-system Nunc Standard Cell Factory systems are built with standard components to help ensure quality and assurance of supply.
Learn more at **thermofisher.com/cellfactory**

Thermo Scientific™ CentriPAK™ BioProcess Container (BPC)

Separate your samples without risk of contamination with the CentriPAK system for the Thermo Scientific™ Sorvall™ BIOS 16 Centrifuge.
Learn more at **thermofisher.com/centripak**

Laboratory Equipment CTS Series

Thermo Scientific™ Laboratory Equipment Packages–Cell Therapy Systems™ (CTS™) Series consist of equipment, a documentation package, and compliance services.

They support your GMP and cleanroom needs for cell and gene therapy manufacturing, and help you get up and running faster, stay compliant, support regulatory audits, and stay on schedule.

- Selected products with high capacity, enhanced cleanability, contamination prevention technologies, and documentation functionalities
- Documentation package including Factory Acceptance Test (FAT) documentation, third-party certifications, as well as recommended protocols
- Compliance services including installation qualification (IQ), operation qualification (OQ) and (depending on product) cycle testing or temperature mapping

Thermo Scientific™ Forma™ Steri-Cult™ CO_2 Incubator–CTS™ Series

Forma Steri-Cult CO_2 incubators offer the ultimate protection for high-value cultures with every element of their design, from the ISO Class 5 HEPA filtration system to their easy cleaning processes and proven automated sterilization cycles. As the largest capacity stackable CO_2 incubator on the market today, the CTS Series supports cell and gene therapy needs from research to high-volume production, providing the documentation critical to validation every step of the way.

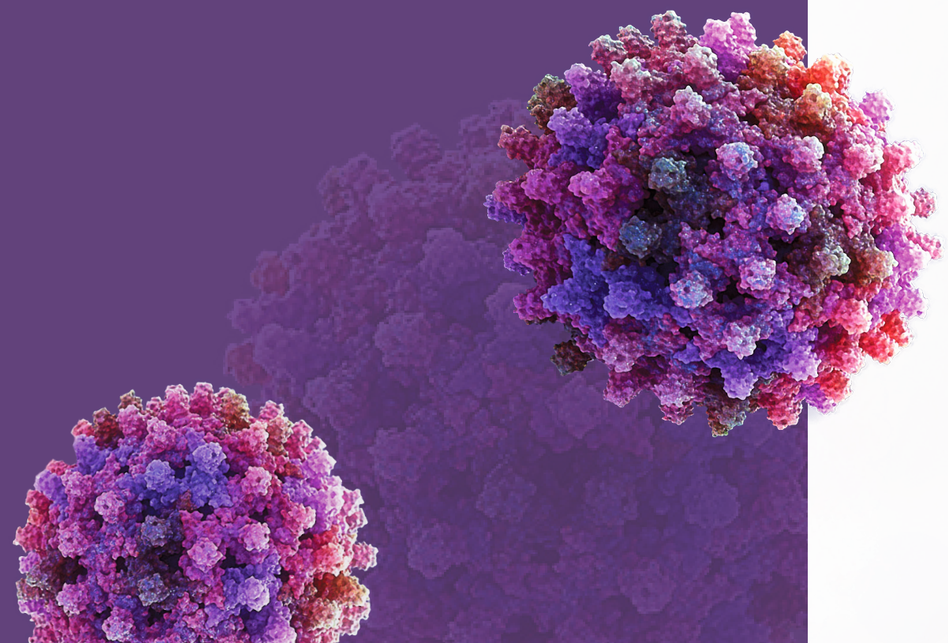
Thermo Scientific™ HeraSafe™ 2030i Biological Safety Cabinet–CTS™ Series

HeraSafe 2030i biological safety cabinets are designed to maximize sample protection and user safety, with an emphasis on containment, comfort, and convenience, all day, every day. The CTS Series includes a comprehensive documentation package, to help save valuable time and giving peace of mind.

VECTOR PURIFICATION

Downstream solutions for viral vectors

Implementing affinity chromatography as the first capture step of viral vectors can bring significant improvement to the downstream process by delivering high yield and purity in a single step. A final polishing step often involves separation of the empty capsids from the full viral particles.



Help reduce time and improve efficiency of your downstream process with CaptureSelect and POROS purification solutions

Thermo Scientific™ CaptureSelect™ affinity products offer a unique affinity purification solution based on camelid-derived single-domain V_HH antibody fragments. Affinity resins enable increased purity and yield in a single step and are designed to simplify workflows, thereby reducing time and cost.

The rigid Thermo Scientific™ POROS™ resin backbone results in highly stable packed beds, as well as a linear pressure flow performance during scale-up. Its high resolution, enabled by a 50 µm pore size, results in tighter peaks and smaller elution volumes, supporting excellent separation of closely related product forms, including empty and full viral capsids.

Options for affinity purification:

ADENO-ASSOCIATED VIRUS

Capture

Thermo Scientific™ POROS™ CaptureSelect™ AAV8, AAV9 and AAVX affinity resins

Polish

Thermo Scientific™ POROS™ IEX resins

LENTIVIRUS

Capture

Thermo Scientific™ POROS™ Heparin affinity resin

Thermo Scientific™ POROS™ D50 resin

Polish

Thermo Scientific™ POROS™ IEX resins

Thermo Scientific™ POROS™ HIC resins

Purification of AAV

Thermo Scientific™ POROS™ CaptureSelect™ AAV resins are unique affinity chromatography resins for the purification of AAV. The CaptureSelect ligand technology, combined with the large pore structure of the POROS beads, enables efficient purification of AAV. In addition, the robust viral clearance capabilities of the resins help to reduce the risk of possible viral contamination derived from the cell culture production process.

The pan-serotype binding property of the AAVX resin provides a key building block for an AAV downstream platform, and could address the rapid process development needs of different serotypes and capsid engineering, as well as transgene combinations.

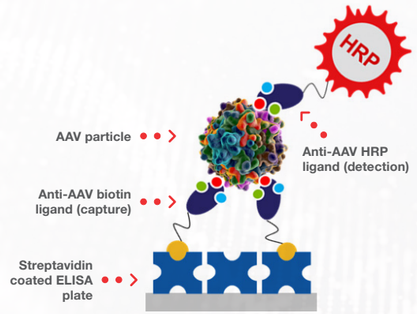
When the use of the final gene therapy product requires further polishing, such as removal of empty capsids, the POROS ion-exchange (IEX) resins can be utilized for subsequent polishing steps. The excellent resolution of these resins allow for efficient separation of closely related product forms, such as empty and full viral capsids.

	5 cm bed height		10 cm bed height	
Diameter (cm)	**7**	**10**	**7**	**10**
Volume (mL)	**190**	**390**	**385**	**785**

Prepacked bioprocess columns for AAV purification

Streamline your AAV purification workflow with Thermo Scientific™ CaptureSelect™ EvolveD™ bioprocess columns:

- Eliminate column preparation and packing
- Ready-to-use formats, suitable for use in cGMP processes
- Suitable for direct connection to standard chromatography systems



Overview of total AAV capsid ELISA using CaptureSelect™ anti-AAV affinity reagents. The biotinylated ligand is used as a capture reagent, while the HRP-labeled ligand is used as a detection reagent.

Labeled AAV affinity ligands for analytical applications

CaptureSelect™ biotinylated and HRP–labeled AAV affinity ligands can be used for the detection and quantitation of AAV. The labeled AAV ligands can be used for various analytical applications, including total AAV capsid ELISA, bio-layer interferometry, surface plasmon resonance, and other immunoassays.

Purification of LV

Anion exchange (AEX) or Heparin affinity chromatography can be used for the purification of lentivirus.

Thermo Scientific™ POROS™ 50 D Weak Anion Exchange Resin and POROS™ Heparin Affinity Resin are high–performance chromatography resins. They are available as media and prepacked columns in a variety of sizes to support every stage from research to production.

Learn how you can save time and increase yields with our wide selection of cell and gene therapy purification solutions at **thermofisher.com/cgt-purification**

Purification buffers and bioprocessing liquids

Accurate and reproducible purification of viral vectors by chromatography, especially ion exchange, requires reagents made under the most stringent conditions. Solutions must also be free of contaminants. Catalog and process liquid and buffer preparations are available with the sizing and packaging you require for optimal productivity.

Learn more at **thermofisher.com/bioprocessing**

LOT RELEASE AND CHARACTERIZATION

Rapid molecular testing for quality and safety

- **Residual DNA quantitation**
- **Mycoplasma detection**
- **Microbial identification**

Patient safety and product quality are fundamental to successful gene therapy. Accurate measurement of process-related impurities and potential microbial contaminants for lot release are critical. In-process analytical testing and environmental monitoring are also essential components of an optimal gene therapy manufacturing process.

Scientists at Thermo Fisher Scientific have developed and validated reliable molecular methods for the rapid and accurate quantification of residual DNA from various host cell and gene-expression systems (Applied Biosystems™ resDNASEQ™ Quantitation Kits), detection of possible mycoplasma contamination (Applied Biosystems™ MycoSEQ™ Mycoplasma Detection System), and identification of possible microbial contaminants (Applied Biosystems™ MicroSEQ™ Microbial Identification System).

Thermo Fisher Scientific provides well-established, sample-to-results solutions to facilitate reproducibility. These include:

- Optimized sample preparation, with our Applied Biosystems™ PrepSEQ™ Nucleic Acid Extraction kits
- Automated sample preparation, including the Applied Biosystems™ AutoMate™ Express and Pharma KingFisher™ Flex systems
- Analytical instrumentation including Applied Biosystems™ QuantStudio™ Dx and Fast Real-Time PCR systems
- Applied Biosystems™ SeqStudio™ and 3500 series genetic analyzers
- Dedicated Applied Biosystems™ AccuSEQ™ data analysis software

Applied Biosystems™ resDNASEQ™ Quantitative DNA Kits are part of an integrated workflow solution to facilitate reproducibility and process development in a GMP environment

AccuSEQ Real-Time PCR Detection Software provides accurate quantitation and security, audit, and e-signature capabilities to help enable 21 CFR Part 11 compliance.

Kits for the detection of residual host DNA

Scientists at Thermo Fisher Scientific have developed various validated resDNASEQ Quantitative DNA Kits for a variety of gene therapy host cell and expression systems. These kits use highly sensitive and specific Applied Biosystems™ TaqMan® Real-Time PCR technology to achieve a broad linear range.

Applied Biosystems™ resDNASEQ™ Quantitative HEK293 DNA Kit

Broad linear range (300 fg–3 ng) and limit of detection of 30 fg of HEK293 DNA in your test samples from a standard curve generated with known amounts of high-quality purified HEK293 DNA standard included in the kit

Applied Biosystems™ resDNASEQ™ Quantitative Sf9 and Bacoluvirus DNA Kit

Duplex assay for the rapid, accurate, and simultaneous quantitation of residual Sf9 host cell DNA and Baculovirus DNA and highly sensitive, with a limit of quantification of 300 fg and limit of detection of 200 fg

Applied Biosystems™ resDNASEQ™ Quantitative *E. coli* DNA Kit

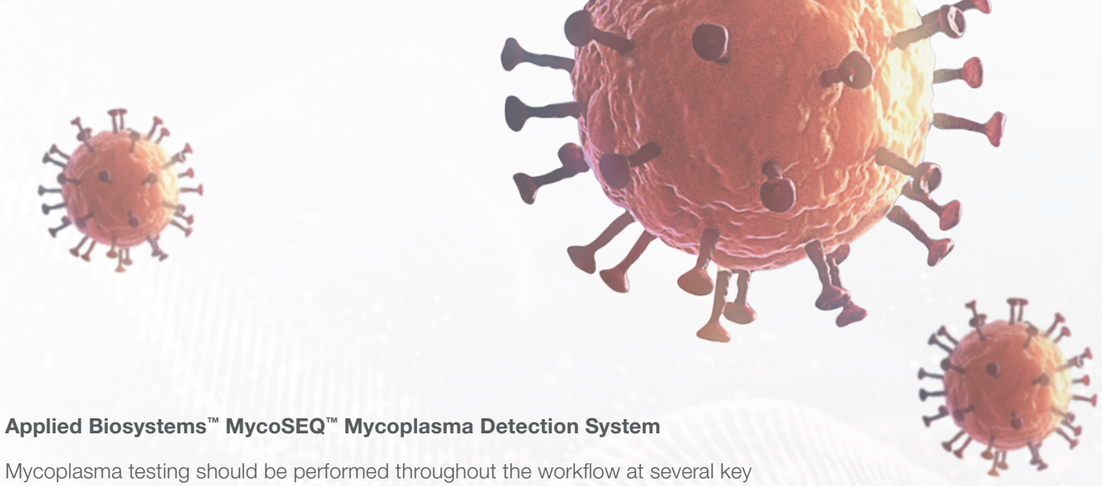
Assay to quantitate residual host cell DNA in common *E.coli*–based plasmid production systems, as well as other *E.coli*–based biotherapeutic processes with a limit of quantitation of 15 pg DNA per mL of test sample in less than 5 hours

Applied Biosystems™ resDNASEQ™ Quantitative Plasmid DNA – Kanamycin Resistance Gene Kit

Multiplexed, highly sensitive, and specific assay for quantifying residual plasmid containing kanamycin resistence genes by targeting all common gene families, with a limit of quantitation of 30 copies and a limit of detection of 15 copies

Thermo Fisher Scientific offers a large portfolio of resDNASEQ Quantitative DNA Kits for other host cell and expression systems.

Learn more at **thermofisher.com/resdnaseq**



Applied Biosystems™ MycoSEQ™ Mycoplasma Detection System

Mycoplasma testing should be performed throughout the workflow at several key points, including cell banking, various stages of scale-up, and harvest, in order to mitigate risk throughout your process. The MycoSEQ Mycoplasma Detection Kit is a real-time PCR assay designed and validated to meet regulatory requirements for lot-release testing in less than 5 hours.

The MycoSEQ Mycoplasma Detection Kit is part of a similar integrated workflow solution as the resDNASEQ kits, including automated sample prep, quantitation instrumentation, and analysis and documentation software.

Learn more at **thermofisher.com/mycoseq**

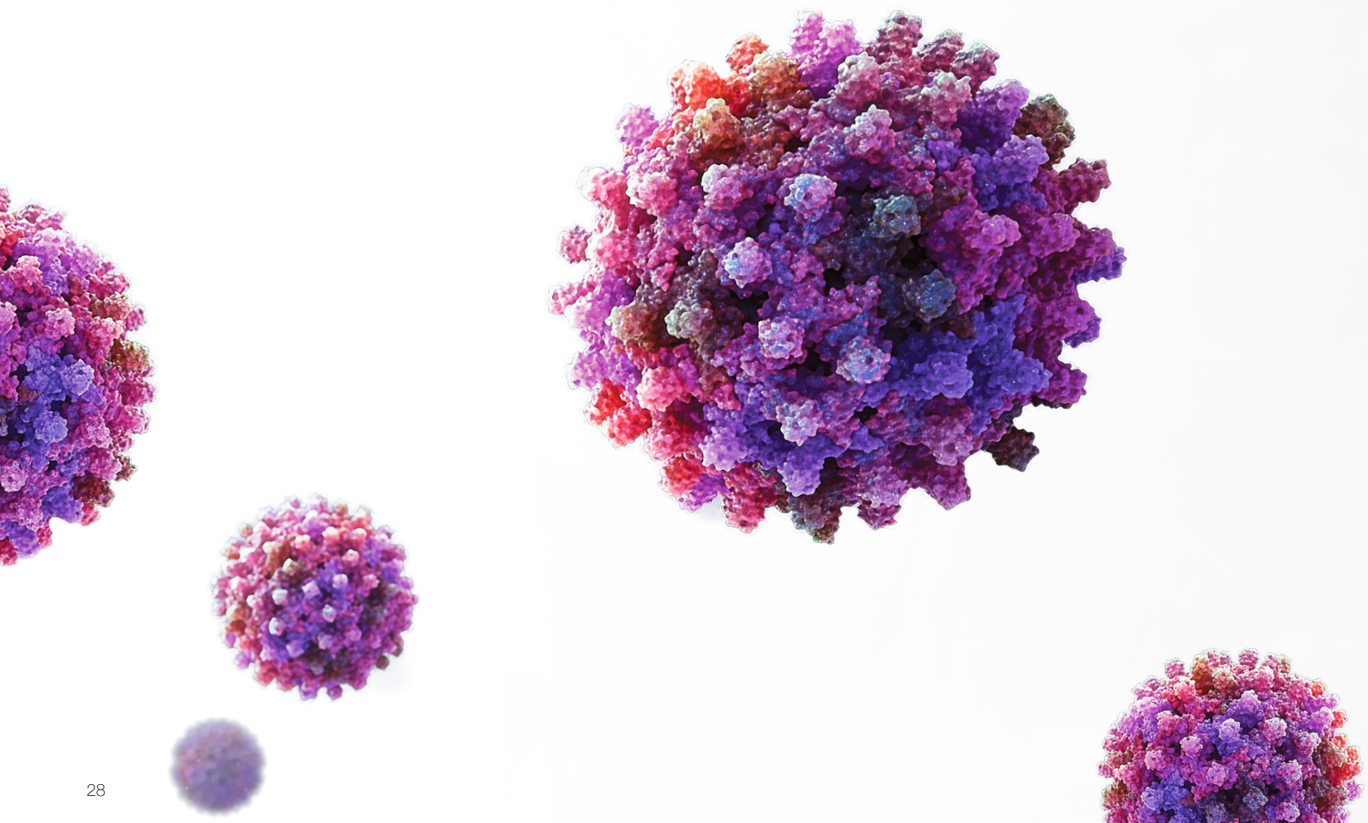
Quickly identify contaminants with the MicroSEQ Microbial Identification System

Test for over 12,000 strain types of bacteria and fungi in about 5 hours using the Applied Biosystems™ MicroSEQ™ Rapid Microbial Identification System. This system delivers precise, actionable results utilizing PCR and DNA.

The MicroSEQ Rapid Microbial Identification System uses a sample-to-answer phylogenetic approach for microbial identification based on the sequencing of the 16S rRNA gene for bacteria or the D2 region of the large subunit ribosomal DNA for fungi.

The MicroSEQ Microbial Identification System is part of an integrated, sample-to-answer workflow solution.

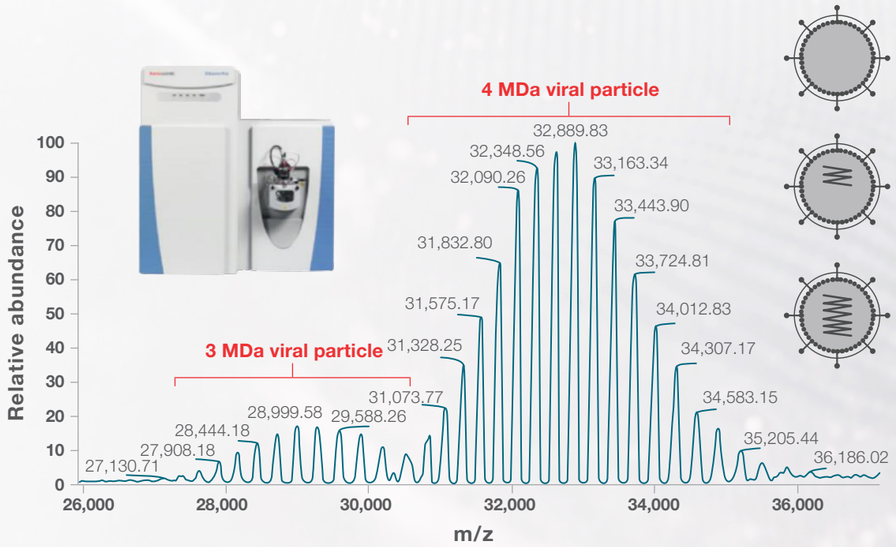
Learn more at **thermofisher.com/microseq**



Comprehensive viral capsid characterization HRAM with extended mass range

Mass confirmation of empty vs. genome–packed capsids can be performed with high confidence using the Thermo Scientific™ Q Exactive™ Ultra-High Mass Range (UMHR) Hybrid Quadrupole-Orbitrap™ Mass Spectrometer.

See how a mixture of 3 MDa and 4 MDa virus capsids analyzed under charge-reducing conditions span a wide mass range between m/z 27,000 and 36,000.



Viral vectors analysis with the Q Exactive UHMR Hybrid Quadrupole-Orbitrap Mass Spectrometer

Learn more at **Gene Therapy Analysis**

FORMULATION, SUPPLY CHAIN, AND LOGISTICS

Quality is a critical component of viral vector production for cell and gene therapies. As a partner with 60 years of experience in manufacturing under cGMP principles, we can connect you to a global network offering guidance and expertise to help you meet regulatory requirements at every step of your journey.

Our robust cGMP supply chain overcomes compliance hurdles to help you succeed in scaling up production and getting your products to market. With 11 state-of-the-art manufacturing facilities worldwide, we can provide a continuous supply of the highest quality product, regardless of location. These sites are ISO 13485– and/or ISO 9001–certified, and FDA-registered. Equipment is cloud-connected, along with a range of informatics and laboratory information management systems (LIMS) to maintain consistency.

Our R&D teams have optimized and developed products designed specifically for viral production

These products strive to enable a seamless transition from research to the clinic by providing scalable products manufactured in conformity with GMP for medical devices, 21 CFR Part 820, following USP<1043> and Ph Eur 5.2.12. Traceability documentation, including Drug Master Files (DMFs), Regulatory Support Files (RSFs), and certificates of origin, are available for these products, along with product safety testing, including sterility, endotoxin testing, and mycoplasma testing on media and reagents.

Find out more

SERVICES

From process development to commercial supply

Chemicals and services

With over 30 years of experience delivering cGMP production chemicals, direct materials, supply chain services, and our production chemical custom packaging services, our Production Chemicals and Services helps biologics developers and manufacturers do what matters most: innovate and produce life-changing therapeutics.

Viral vector production services

Patheon™ Viral Vector Services (VVS), a part of Thermo Fisher Scientific, is your end-to-end viral vector contract development and manufacturing organization (CDMO) partner from process and analytical development to clinical and commercial supply of viral vectors for gene therapy. Our team acts as an extension of your team, operating with transparency and flexibility to keep you involved, engaged, and well-informed at every stage. With 20 years of experience developing processes and producing over 60 cGMP viral vectors: including AAV, adenovirus, lentivirus, herpes simplex virus (HSV), and retrovirus, we can help you overcome challenges associated with these complex products. Quality is at the core of everything we do. We strive to exceed our clients' expectations on every project while ensuring regulatory compliance and the highest product quality possible. Learn more about our viral production services at **thermofisher.com/patheon**

cGMP plasmid manufacturing services

Bring your gene-based therapies to market without sacrificing critical timelines. You can rely on our manufacturing experience to ensure commercial-quality GMP plasmid DNA for cell and gene therapies right from the start—avoiding transitions in material quality and saving manufacturing time. We have the capacity, manufacturing processes, analytical capabilities, and technical expertise to allow you to move quickly from clinical trials to commercial supply. Our state-of-the-art production suites in multiple manufacturing locations are dedicated to commercial-quality GMP plasmid production, providing you shorter lead times and flexibility in manufacturing timelines when there are changes in your schedule. Learn more about our plasmid manufacturing services at **thermofisher.com/patheon**

Global supply solutions and logistics

Beyond our complete viral vector production and cGMP plasmid services, we also offer global clinical supply solutions for every trial. Our dedicated and experienced team are committed to delivering end-to-end, high-quality, global clinical supply chain services to clinical researchers and patients around the world. Whether you need primary or secondary packaging of your clinical drug, storage, distribution, logistics, cold chain management, or comparator and ancillary sourcing, our global team can meet the needs of your trial regardless of size, phase, or therapeutic area. We also offer import and export services, including Importer of Record (IOR) capability in more than 25 countries (to date,) and best-in-class direct-to-patient services. Learn more at **patheon.com/clinical-trial-services** and **patheon.com/logistics-services**

Bioproduction services

With over 60 years of experience developing industry–leading media, you can rely on the Gibco team to help you achieve optimal performance. Accelerate your gene therapy development and production for increased market impact of your life–saving therapeutics. As a leader in quality, innovation, and capacity, we are equipped to efficiently meet your demand, no matter the scale. With expertise in media manufacturing, scalable solutions and format conversion, our proven team and leading services can help enhance your workflows. From non-GMP media prototyping to manufacturing your own formulation for production and custom packaging we can support your entire media manufacturing journey.
Visit **thermofisher.com/bioprocessing**

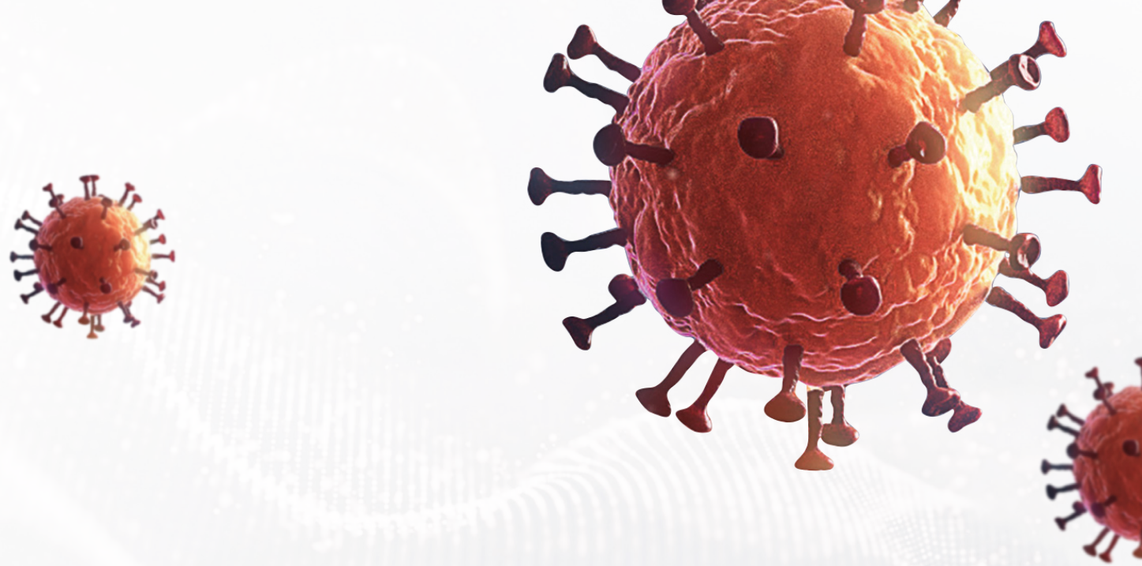
Custom chromatography services

To help ensure you meet your timelines, we offer a unique, milestone-based service for the development of specific affinity solutions that are tailored to a target protein and its specific requirements. The custom ligand can be immobilized on a variety of backbones, including POROS™ resins, and further developed into an affinity resin, which can be used in large-scale processing of biopharmaceuticals.

Custom POROS resins

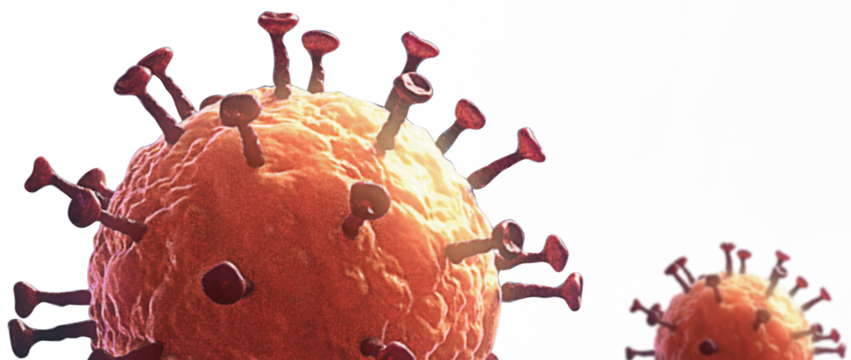
Simplify your workflow and reduce manufacturing time and cost with our POROS technology. POROS chromatography resins provide attributes that are well-suited to downstream processing. With our resin development program, you'll receive a high-speed, high performance chromatography solution tailored to your process requirements. Learn more at **thermofisher.com/custom-chromatography-solutions**

PROFESSIONAL SUPPORT FROM EARLY DISCOVERY TO PRODUCTION



For the life of your therapeutic, from early discovery through production, Thermo Fisher Scientific partners with our clients to provide flexible solutions that optimize quality, service, and cost while delivering results. Our team includes thousands of professionals including:

- Regulatory support specialists to help you anticipate and navigate regulatory steps, from research through commercialization
- Specialized regional technical support and field support teams to provide detailed product support and consultation, as well as customization of products, with both remote and on-site consultations
- Project managers to manage scope, mitigate risk, manage timelines, and capture key decisions and action items to help ensure projects achieve your goals and are completed on time
- R&D scientists continuously develop new products and improve existing favorites to meet your development needs today, while building an effective framework for future success
- Global business development managers leverage their extensive knowledge of biotech business modeling and life science investment evaluation to craft agreements that are mutually beneficial and efficient, and teams also connect our clients to the many resources within Thermo Fisher Scientific



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[2] Martínez-Molina, E., Chocarro-Wrona, C., Martínez-Moreno, D., Marchal, J. A., and Boulaiz, H. (2020). Large-Scale Production of Lentiviral Vectors: Current Perspectives and Challenges. Pharmaceutics, 12(11), 1051.

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ADVANCING YOUR GENE THERAPY FROM DISCOVERY TO PATIENT REALITY

Contact us today to find out how we can support and guide your projects, keep you agile, and help meet your needs to advance your therapeutic.

Find out more at **thermofisher.com/genetherapy**