

## Life science research solutions

Services to accelerate your scientific research



## Life science research services

When your project and timelines require specialized, reliable, high-quality solutions, you can count on our team of experienced professionals to help plan the best opportunities for your research goals and deliver.

Our wide range of service capabilities leverages an industryleading portfolio of equipment, technologies, and competence built by the most recognized life science brands in the world.

As you review this handbook, keep in mind that we can partner with you on almost any type of research and offer custom solutions to meet short timelines or complex problems, or overcome gaps in technical skills. We are looking forward to working with you on your next big discovery.



## Our leading scientific products, services, and workflow solutions

thermo scientific

Enabling analytical precision and diagnostics excellence

**fisher** scientific

One-stop access for scientific products

**applied** biosystems

Inspiring meaningful genetic analysis

**unity** lab services

Instrument and enterprise services

invitrogen

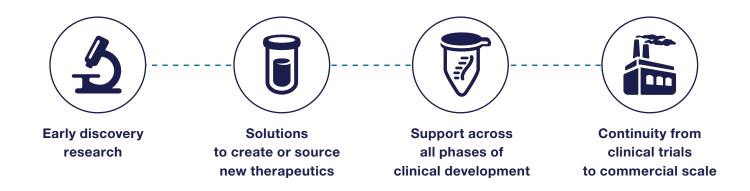
Accelerating discovery research

patheon

Solutions for drug development, clinical research logistics, and commercial manufacturing



## Your partner at every step in your therapeutics journey



To attain market success by improving health outcomes, Thermo Fisher Scientific is the one partner you need.

From discovery to commercialization, Thermo Fisher Scientific provides competence and a superior array of scalable tools, services, and support, designed to deliver high-quality results and accelerate your productivity and innovation.

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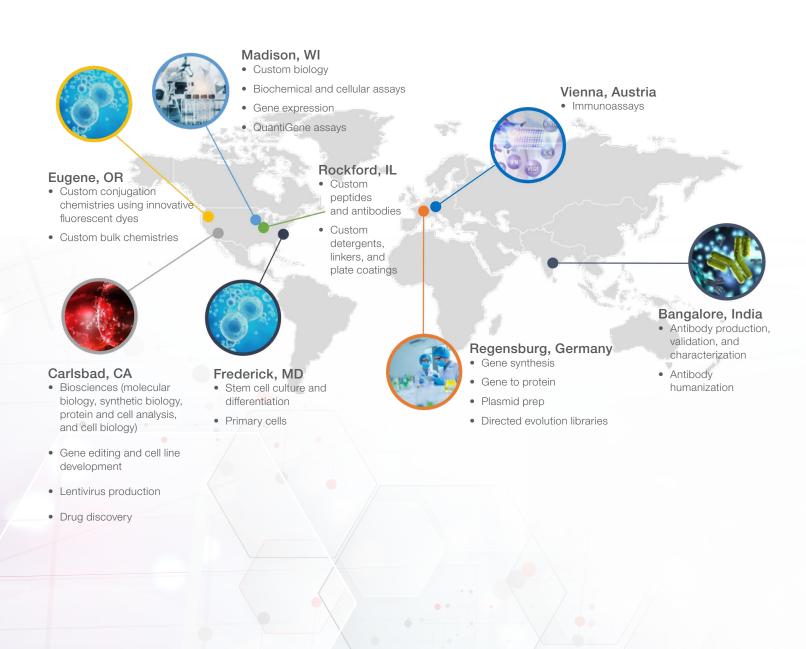


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Learn more at thermofisher.com/services

## Our R&D network

## Our custom services team leverages the global Thermo Fisher Scientific R&D network



## Our aim is to improve your results and accelerate your success

We can help you reach your goals

We want to support your outsourcing needs, and whether your needs are utilizing our competence or scaling technologies to meet demand, we can help you at every step.

**Proprietary solutions**—we use our own equipment and products, allowing you the flexibility to transfer any project directly to your facility or lab

**Experienced professionals to support your research goals**—direct support from the R&D teams that developed the reagents, instruments, and tools used at the bench

**Collaboration as partners to drive discovery**—our R&D breakthroughs are translated into service offerings

**Trusted products for quality, cutting-edge solutions**—our service offering is built on 30 years of industry-leading innovation

## **Testimonials**

## From current and past service partners

"Overall, I felt the project manager was very responsive and able to answer all my technical questions. She provided clear instructions for sample submission and also sent helpful brochures on the technology we used."

"The overall service was super prompt, and very detailed and helpful. I would highly recommend the services; the entire procedure is well explained, and it's very fast and reliable."

"I have already recommended to another colleague to use Thermo Fisher. Service is usually run smoothly and professionally."

"All my inquiries before/during/after the test were answered with sufficient details and in a timely manner."

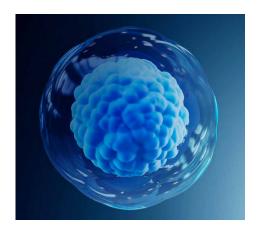
"Broad, diverse array of services ... they are consistently an industry standout in project management and customer service."

"I really, really like the new email notifications I'm getting that announce partial data availability. Thank you to everyone who contributed to this new online data system!"

"Very responsive and gave detailed answers to my questions. Felt very trustworthy and I felt like he really cared about me as a customer, even though my project was relatively small."



"High-quality data, numerous assays offered in the portfolio"



"Great service, great response times, very easy-to-use portal"



## Cell engineering services

At Thermo Fisher Scientific, we have a complete toolbox comprising trusted solutions to support every step in the cell engineering workflow. Using our collection of the most robust and reliable technologies on the market, our scientists will work with you to design custom projects to meet your requirements. Whether you want custom stable cell lines or expression tools, we have the technologies and expertise to support your cell engineering needs.

Read through the following pages to better understand how our cell engineering services can expedite your current projects, or find out more at

thermofisher.com/engineeringservices

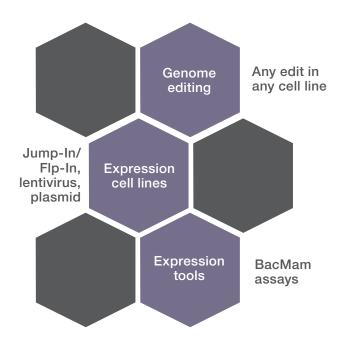


## Complete cell engineering solutions

With our cutting-edge technologies and experience, we can help build the tools you need to create more relevant disease models for your projects.

## Decades of experience to support your cell engineering needs

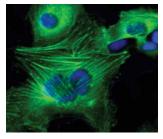
- Leverage our experience to boost your R&D productivity with our end-to-end cell line generation services
- Our team has the skills and experience to provide any edit in any cell line
- With over 15 years of experience, we have generated thousands of cell lines for our customers using standard cell lines, primary cells, and stem cells
- From knockouts to knock-ins and overexpression models, we can take on the burden of cell line production, freeing your team to focus on discovery



## Genome editing

Creating stable cell lines is time-consuming and complex. The trusted, experienced developers of Invitrogen™ GeneArt™ TALs and GeneArt™ CRISPR products can custom-design stable cell lines using one of the most robust and reliable technologies on the market.

Utilizing quality products throughout the process, our scientists will work with you to design the stable cell line you want and perform quality-control testing to help ensure that the cell line meets your requirements.



C-terminal ACTB EmGFP

### A typical genome editing service workflow is shown below:



### **Design and build**

Design your experiment and assemble the optimal set of tools

- gRNA design and synthesis
- Invitrogen™ GeneArt™ PerfectMatch TAL effectors
- Invitrogen<sup>™</sup> GeneArt<sup>™</sup> gene synthesis and oligos for donor DNA
- Invitrogen<sup>™</sup> TrueCut<sup>™</sup> Cas9 Protein v2



#### **Deliver**

Highly efficient delivery of editing tools to the cells

- Transfection optimization
- Transfection



### Screen, isolate, and expand

Screen, isolate, and expand clones to identify those with modifications

- Single-cell sorting
- Clonal screening
- Expansion of clones



### **Validate**

Confirm gene editing by Ion Torrent™ sequencing, protein knockout, and functional assays

- Sequence confirmation using next-generation sequencing (NGS)
- On-/off-target analysis
- Functional characterization
- Stem cell characterization

### **Award-winning tools**

We utilize award-winning genome editing tools and reagents in our service.

### Any edit in any cell line

We have generated thousands of edited cell lines for our customers.

### **Every editing project is unique to the client**

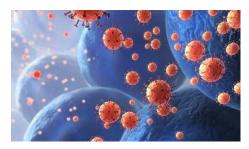
We offer consultation services to evaluate the technical feasibility of editing in your desired cell line.

#### **Customized solutions**

Completely customizable solutions to ensure the edited cell lines meet your needs.

## Tools and services for generating expression cell lines

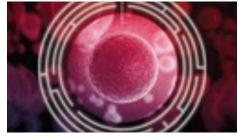
### Solutions for maximum flexibility



### **Expression tools**

Invitrogen<sup>™</sup> BacMam<sup>™</sup> virus and lentivirus production service

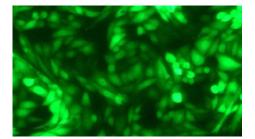
- Available: lentivirus, BacMam vector
- Gene synthesis, cloning, virus packaging



### **Traditional cell lines**

Traditional cell line generation with total flexibility in cell background of choice

- Available in all cell backgrounds
- Options: lentivirus, plasmid



Invitrogen<sup>™</sup> Jump-In<sup>™</sup> and Flp-In<sup>™</sup> technology

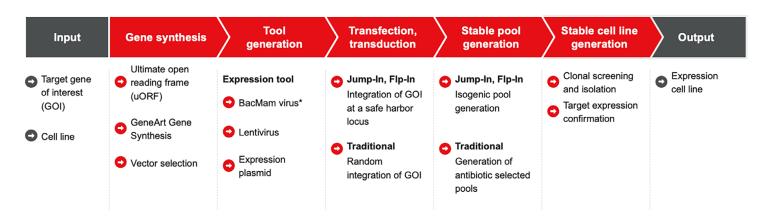
Cell pool with a gene of interest integrated at a defined genomic locus

- Isogenic pool in as little as 5 weeks
- Jump-In/Flp-In parental cell lines available

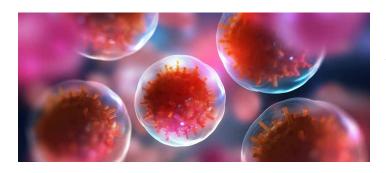
### Service workflow for generating expression tools and cell lines

### Standard expression cell line generation

The size and experience of our team gives you the flexibility to start and stop at any step in our services workflow. Outsource basic steps or complex ones, depending on the unique needs of your projects—learn more about our expression workflow below.



### The BacMam system



### BacMam virus generation

endothelial cell

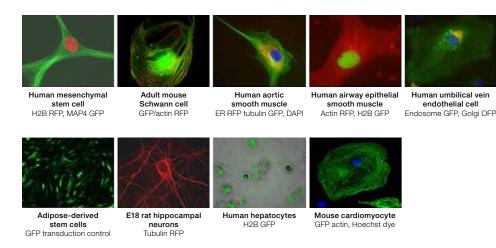
The BacMam virus generation service enables production of baculovirus for an efficient, covenient, and safe method of gene delivery. The BacMam system has high expression levels, is nontoxic to cells, and is platform-agnostic.

Safety Nonreplicating in mammalian cells

**Portability** Demonstrated transduction in hard-to-transfect cells, e.g., primary and stem cells

Easy-to-use workflow Enables batch transduction

The BacMam system is compatible with multiple cell types and can be used to transduce hard-to-transfect cells.

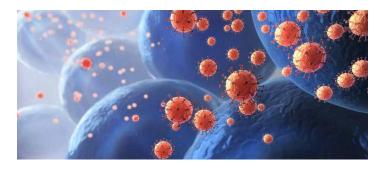


With our BacMam virus generation service, we can generate a BacMam virus with your gene of interest in as little as 5 weeks.

Simply provide us with your gene of interest and select a desired BacMam virus volume ranging from 100 mL to 1 L.

### Lentiviral services overview

## Packaged and titered lentivirus available in as little as 3 weeks



### Complete solution

End-to-end service for lentivirus production

### Breadth of options

Different promoters and selection markers available for maximum flexibility; we can also accept customer's vector

### Quick turnaround time

Packaged and titered lentivirus ready in as little as 3 weeks

### **Lentiviral production service**

We offer a complete end-to-end service for the creation of lentiviral expression constructs and packaging.

### **Gene synthesis**

- GeneArt proprietary codon optimization algorithm maximizes expression of gene of interest
- Gene can be synthesized and cloned into the vector backbone of interest
- Deliverable in various sizes—mini, maxi, or mega prep

### Lentivirus packaging

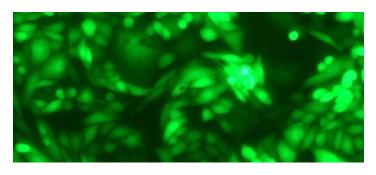
- Uses state-of-the-art
   Gibco™ LV-MAX™ system
- Packaged virus particles can be concentrated up to 100x

### **Titer**

- Virus production measured by p24 ELISA assay
- Functional titer using selection marker or fluorescent marker; available as a separate assay

## Jump-In/Flp-In services

Integration of genetic material at a defined genomic site in as little as 5 weeks



Isogenic expression

Gene of interest targeted to and expressed from a defined genomic locus

### Efficiency

Functional cell pools can be generated in as little as 5 weeks

### Large inserts

Accepts large multigene inserts

### Invitrogen™ Jump-In™ and Flp-In™ cell line generation

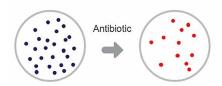
Jump-In and Flp-In services enable the rapid generation of an expression pool of cells with a gene of interest integrated at a defined target genomic locus.



### Stable transfection

### Foundational tools:

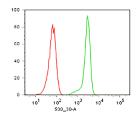
- Host cell lines
- Invitrogen<sup>™</sup> Gateway<sup>™</sup> targetable vector
- Jump-In service: R4 integrase Flp-In service: recombinase vector



### **Antibiotic selection**

### Steps:

· Selection with blasticidin or hygromycin (~3 weeks)



### Isogenic cell pool

### Steps:

- Validation of protein expression, assay performance, etc.
- Validation of R4 integration by PCR

### Select from our catalog of Jump-In and Flp-In parental cell lines

- Jump-In CHO-K1
- Jump-In GripTite HEK293
- Jump-In HEK293
- Jump-In K562
- Jump-In T-REx CHO-K1

- Jump-In T-REx HEK293
- Jump-In T-REx U2OS
- Jump-In Tango UAS-bla U2OS
- Flp-In CHO-K1
- Flp-In CV-1

- Flp-In HEK293
- Flp-In BHK
- Flp-In 3T3
- Flp-In Jurkat
- Flp-In T-REx HEK293

### Don't see the Jump-In parental cell lines you need?

We can generate custom Jump-In host cell lines for you.

Find out more at thermofisher.com/engineeringservices

## Case study

See how our engineered cell line services can accelerate key discoveries, with real-world applications

### **Article**

## The clinical KRAS(G12C) inhibitor AMG 510 drives anti-tumour immunity

https://doi.org/10.1038/s41586-019-1694-1

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Jude Canon<sup>1\*</sup>, Karen Rex<sup>1,17</sup>, Anne Y. Saikl<sup>1,17</sup>, Christopher Mohr<sup>1</sup>, Keegan Cooke<sup>1</sup>,
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Jayesh Desal<sup>10</sup>, James Kuo<sup>11</sup>, Ramaswamy Govindan<sup>12</sup>, David S. Hong<sup>13</sup>, Wenjun Ouyang<sup>2</sup>,
Haby Henary<sup>4</sup>, Tara Arvedson<sup>2</sup>, Victor J. Cee<sup>1</sup> & J. Russell Lipford<sup>1\*</sup>

### **Summary**

An engineered CT-26 KRAS p.G12C cell line contributed to the discovery of the novel AMG 510 as the first KRAS(G12C) inhibitor in clinical development.

Nature 575:217–223 (2019). https://doi.org/10.1038/s41586-019-1694-1

### Input

Murine CT-26 colorectal line

### Gene modification

Confirm both KRAS alleles as G12D via NGS

Replace Replace using

Replace with G12C using CRISPR-Cas9

### Output

Engineered CT-26 KRAS p.G12C cells

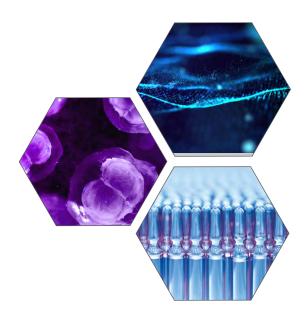


## Stem cell services

Built on decades of stem cell experience and the comprehensive Thermo Fisher portfolio of products and equipment, our CellModel™ Services offer you flexibility and assistance with any stage of your stem cell research. Find out more about our services on the following pages, or reach out to our team of scientists to inquire about any custom projects or standard services for stem cell reprogramming, differentiation, characterization, and analysis.

Find out more about our stem cell services at

thermofisher.com/cellmodels



## Offerings





### Reprogramming

Reprogram your human fibroblasts or blood cells to PSCs

Reprogram human fibroblasts or blood cells and provide pluripotent stem cells (PSCs) to you in 4–6 months.

Choose from two non-integrating reprogramming technologies:

- Invitrogen™ CytoTune™iPS 2.0 Sendai Reprogramming Kit
- Invitrogen<sup>™</sup> Epi5<sup>™</sup>
   Episomal iPSC
   Reprogramming Kit



#### **Engineering**

Introduce diseaserelevant mutations or indels to your PSCs

Custom-design stable stem cell lines using the most robust and reliable editing technologies on the market.

Award-winning editing tools:

- Invitrogen™ GeneArt™ CRISPR-Cas9 products
- Invitrogen™ GeneArt™ Precision TALs

Modification options:

- Knockouts, SNPs
- Large knock-ins



#### Differentiation

Differentiate your PSCs to your desired terminal cell type

Stem cell differentiation projects are typically completed within 4–8 weeks from project initiation.

Available cell types:

- Dopaminergic neurons and progenitors
- Central nervous system (CNS) neurons and progenitors
- Cardiomyocytes
- Custom



### Assay development

Develop and optimize custom assays to support drug discovery and development

A broad range of assay tools and instrumentation that can be implemented with PSCs or their differentiated progeny to interrogate diseaserelevant biology.

- Cell viability
- Cell proliferation
- Apoptosis
- Pathway signaling
- Gene and protein expression
- Posttranslational modifications
- Custom



#### Screening

Screen compounds using our high-throughput screening facility

We also offer stem cell screening services to enable rapid profiling of your compounds against many assay technology platforms through our SelectScreen" team and services.



#### Characterization

Robust tools to characterize your PSCs, or differentiated cell types, anywhere throughout the process

### Genomic analysis

- Applied Biosystems<sup>™</sup> KaryoStat+ Karyotyping Service
- Ion Torrent™ Oncomine™ service
- KaryoStat and cell identification service

### Pluripotency

- PluriTest<sup>™</sup> service
- Applied Biosystems<sup>™</sup> TaqMan<sup>®</sup> hPSC Scorecard service
- Tri-lineage differentiation service

### Sterility

• Mycoplasma detection service

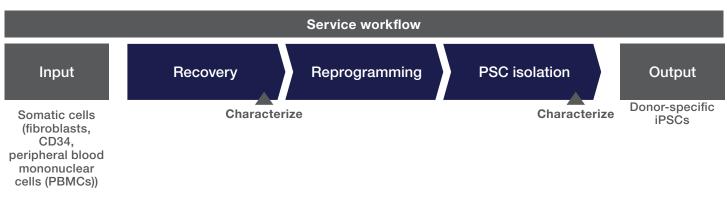
**Note:** We are continually expanding our service capabilities and offerings. Please reach out to your local sales specialist to see how we can help achieve your project goals.

## Overview of reprogramming services

Generate iPSCs from your donor of interest

Our CellModel™ Stem Cell Reprogramming Services enable the conversion of human fibroblasts or blood cells to induced PSCs (iPSCs) in 4-6 months using either of our non-integrating reprogramming technologies, with top clones expanded, cryopreserved, and characterized.





Find out more at thermofisher.com/stemcellservices

## Overview of genome editing service

We leverage our award-winning tools in our Stem Cell Genome Editing Service to introduce specific mutations into the genome of your iPSCs or our Gibco™ iPSC line.

Design and build	Deliver	Stable pools	Stable clones	Validate
Design your experiment and assemble the optimal set of tools  • gRNA design and synthesis  • PerfectMatch TAL effectors	Deliver editing tools to the cells in a highly efficient manner  Transfection optimization  Transfection	Expand pools with modifications as requested • Expansion of pools	Screen, isolate, and expand clones to identify those with modifications  • Single-cell sorting  • Clonal screening  • Expansion of clones	Confirm gene editing by Ion Torrent™ NGS, protein knockout, and functional assays  • Functional characterization  • Stem cell characterization
Invitrogen™ GeneArt™ Gene Synthesis and oligos for donor DNA				<ul> <li>Sequence confirmation using NGS</li> </ul>

## Case study

iPSCs engineered as hypoimmunogenic graft for universal transplantation



## Hypoimmunogenic derivatives of induced pluripotent stem cells evade immune rejection in fully immunocompetent allogeneic recipients

Tobias Deuse<sup>1,7</sup>, Xiaomeng Hu<sup>1,2,3,7</sup>, Alessia Gravina<sup>1</sup>, Dong Wang<sup>1,2</sup>, Grigol Tediashvili<sup>1,2,3</sup>, Chandrav De<sup>4</sup>, William O. Thayer<sup>4</sup>, Angela Wahl<sup>4</sup>, J. Victor Garcia<sup>4</sup>, Hermann Reichenspurner<sup>2,3</sup>, Mark M. Davis<sup>5</sup>, Lewis L. Lanier <sup>©</sup> and Sonja Schrepfer <sup>©</sup> 1\*

### Research goal

To generate hypoimmunogenic iPSCs through the inactivation of MHC class I and II genes and overexpression of CD47 for universal transplant.

Nat Biotechnol 37:252-258 (2019).

### **Grow cells**

### **Engineer**

### Differentiate

### Analyze in vivo



Customer conducted this study first with mouse iPSCs and later with human iPSCs

- Mouse iPSC (customer supplied)
- Human iPSC (Gibco Cas9 iPSC)



Our CellModel Services team then generated hypoimmunogenic iPSC models by performing:

- Knockout of MHC class I and II genes (B2M and CIITA) using CRISPR-Cas9 technology
- Overexpressed CD47 gene using viral transgenic approach



Using the engineered cell lines, our customer differentiated them into endothelial-like cells and cardiomyocytes for downstream *in vivo* study.

Our service team can also perform differentiation through our CellModel Stem Cell Differentiation Services.



The differentiated cells were used as cell grafts in a transplant study and evaluated for survival and structural change in allogeneic recipients.

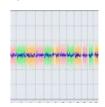
Find out more at thermofisher.com/stemcellservices

## Essential services for the characterization of stem cells

It is important to characterize your stem cell lines, especially after stressful interventions such as genome editing or clonal isolation. We offer a suite of characterization solutions for qualification of your stem cells. Most characterization projects are completed in 2–4 weeks.

### **Genomic analysis**

### KaryoStat+ service



An alternative to G-band karyotyping of stem cells, our KaryoStat+ service offers cost-effective and accurate detection of chromosomal abnormalities in stem cells.

### Oncomine service



Leverages our Ion Torrent NGS platform to monitor samples for genomic variations associated with cancer hotspots (recognized by National Institutes of Health (NIH)).

### KaryoStat and cell identification service



Leverages CytoScan array to generate a donorunique fingerprint of human cells. This service can be used to track cell identity during cell engineering or long-term experiments.

### **Pluripotency**

### PluriTest service



Using our Applied Biosystems™ PrimeView™ Human Gene Expression Array, we analyze over 36,000 transcripts and variants for global assessment of pluripotency.

### TaqMan hPSC Scorecard service



Leverages our TaqMan Scorecard system, an optimized panel of 93 genes, to confirm pluripotency and differentiation potential of edited iPSCs.

### Trilineage differentiation service



Through unbiased differentiation of PSCs, the differentiation potential of a PSC line can be assessed. Embryoid bodies (EBs) are generated and analyzed on the TaqMan Scorecard system to evaluate germ layer differentiation potential.

### **Sterility**

### Mycoplasma service



A service that leverages the Applied Biosystems<sup>™</sup> MycoSEQ<sup>™</sup> Mycoplasma Detection Kit to detect over 90 mycoplasma species in samples—simply, reliably, and rapidly.

All services are available as stand-alone projects or as integrated milestones in cell line generation services.

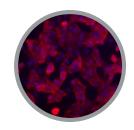
### Learn more at thermofisher.com/characterizationservices

### Overview of differentiation service

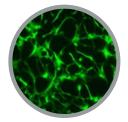
Our differentiation service enables the specification of PSCs to diseaserelevant cell types. Using our proprietary differentiation technologies, we can generate a range of cell types from PSCs in as little as 3-6 weeks.



Dopaminergic (DA) neurons and progenitors



Cardiomyocytes



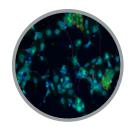
CNS neurons and progenitors



Terminally differentiated custom cell types

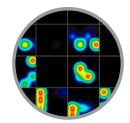
## Overview of analysis capabilities

Thermo Fisher Scientific has extensive products and applications to support your post-differentiation analysis requirements.



### High-content analysis

- Cell health and morphology
- Neurite outgrowth
- Culture characterization



### **Functional assays**

- Calcium release assays
- Voltage reporters
- Multi-electrode arrays



### **Custom analysis**

Please inquire with your project manager for a feasibility assessment.

Find out more at thermofisher.com/stemcellservices

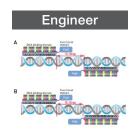
### Use of our CellModel Services in case studies

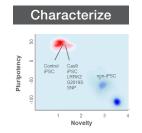
### Case study 1: Parkinson's disease model generation

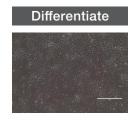
### Parkinson's disease model generation

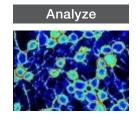
- Understand the molecular basis of Parkinson's disease
- Identify compounds that can impact disease phenotypes

# Short and short street short st









LRRK2 G2019S mutant iPSCs generated using Gibco Cas9 iPSC with high efficiency Pluripotency and karyotype of edited cells were unaffected by genome editing DA neurons successfully differentiated from *LRRK2* G2019S mutant iPSCs

LRRK2 G2019S mutation in DA neurons affected neurite outgrowth, neurotoxin sensitivity, and gene expression

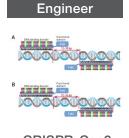


### Case study 2: Model development for dilated cardiomyopathy

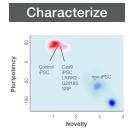
### Cardiomyocyte disease modeling

- Introduce TNNT2 R141W mutation into iPSCs to mimic dilated cardiomyopathy (DCM)
- Differentiate into cardiomyocytes and characterize to confirm functionality of model





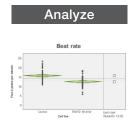
CRISPR-Cas9 gene editing TNNT2 R141W mutation



Characterization of engineered iPSCs



Cardiomyocytes



Cell-based assays
Calcium transients
Beat rate

## Drug discovery

At Thermo Fisher Scientific, our scientists can help you do more by providing services that enable predictive answers for drug discovery research. With dedicated technical support specialists and a team of R&D scientists in screening, kinase profiling, and custom assay development, we can help you extend your research capabilities or expedite a step in your workflow.

Read through the following pages and find out how our technologies and expertise can help you today, or visit our website at **thermofisher.com/drugdiscovery** 

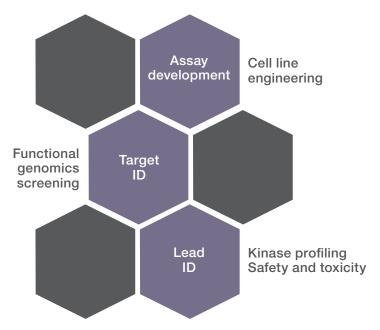


## Overview of our drug discovery and development capabilities

By leveraging our drug discovery capabilities and competence, we can provide the support you need for your drug discovery and development workflow.

#### Statistics:

- 10 functional genomics screens
- >50 assay development projects completed
- >28,000 profiling projects completed since 2004



Extensive drug discovery and development capabilities for your discovery needs



Create relevant test system to identify target and evaluate effects of compounds on target

- Cell engineering
- Assay development

Identification of target and linkage of target to disease

• Functional genomics screen

Rapid identification of "active" compounds

- Cell banking
- SelectScreen services
  - Kinase profiling
  - Library screen

Demonstrate efficacy in cellular models and optimize specificity and safety of drug

- SelectScreen services
  - Kinase profiling
  - P450 profiling
  - hERG screening

## Custom assay development

We offer a wide array of screening technologies and systems to help you create custom assay solutions. Find out more about how we can partner today.

### The custom assay development process

Using tools that our scientists created, coupled with our experience in applying that technology, we provide custom solutions to meet your unique assay requirements.

Step 1: Identify the problem	Step 2: Develop the solution	Step 3: Manage tasks and report results
Customer identifies needs	Custom team evaluates the best technology and approach	Custom team manages project milestones and reporting
Customer provides information about:  • Target protein or pathway	Customer-centric biology team: Suggests a delivery or expression system for target protein based on cell background and downstream use	Custom biology team provides Milestone Reports that include:  • Experimental goals  • Materials
A biological problem	Proposes methods to clone or synthesize a target	Methods
Target modification or biological function	Generates a virus or cell line	• Results
<ul> <li>Suggested antibodies, if appropriate</li> </ul>	<ul> <li>Identifies and labels antibodies, if appropriate</li> <li>Tests the labeled antibodies and the cell line or the virus used to induce expression in the cell line</li> </ul>	Plus a Final Milestone Report and set of deliverables that include:  • Custom reagents
Cell background	<ul> <li>Tests the custom reagents (virus, antibodies, or cell line) in the appropriate assay format</li> <li>Elicits customer involvement as needed</li> </ul>	<ul><li>Protocol to enable running assays in your own lab</li><li>Lists of required catalog materials</li></ul>
Expectations:	Freedom to operate:	Deliverables:
Describe expected downstream use	Ask about our capabilities beyond our own portfolio of products*	• Milestone and Final Milestone Reports, cell lines, antibodies, etc.

<sup>\*</sup> If you would like to request a technology outside of the Thermo Fisher Scientific portfolio, please inquire about this process at discoveryservices@thermofisher.com.

Thermo Fisher has a wide range of technologies that can be leveraged to create customized solutions to support your high-throughput screening needs. From biochemical to cellular formats, assay development has been at the core of our business for over 15 years.

Reach out and find out more about how we can partner with you to build customized assay solutions.

Find out more about biochemical assay development at **thermofisher.com/biochemassay** 

Thermo Scientific <sup>™</sup>	Thermo Scientific <sup>™</sup>	Thermo Scientific <sup>™</sup> nuclear receptor (NR) assays	Invitrogen <sup>™</sup>
kinases	GPCR assays		ion channels
<ul> <li>Purified kinase proteins</li> <li>Biochemical assays         <ul> <li>LanthaScreen™</li> <li>Z'-Lyte™</li> <li>Adapta™</li> </ul> </li> <li>Cellular assays         <ul> <li>CellSensor™</li> <li>LanthaScreen</li> <li>BacMam</li> </ul> </li> </ul>	<ul> <li>CellSensor cell line</li> <li>Tango™ cell lines</li> <li>GeneBLAzer™</li> <li>Second messenger readouts</li> <li>Calcium flux (fluo-4)</li> </ul>	<ul> <li>Purified NR proteins</li> <li>Biochemical assays         <ul> <li>PolarScreen™</li> <li>LanthaScreen</li> </ul> </li> <li>Cellular assays         <ul> <li>GeneBLAzer</li> </ul> </li> </ul>	<ul><li>hERG</li><li>FluxOR</li><li>Voltage sensor probes</li></ul>

Find out more at thermofisher.com/drugdiscovery

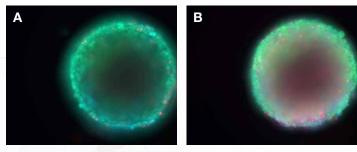
### 3D cell model services

Our industry-leading portfolio of research services now has added 3D cancer spheroid models to allow you to identify new targets or lead compounds. Leverage our team of experienced professionals to take on some of your most challenging (or mundane) work.

### Our new cancer model services offer:

- A single source for genome editing, 3D culture, and custom assay development
- Access to 28 cancer cell models, including:
  - LNCaP (prostate)
  - MCF-7 (breast)
  - A549 (lung)
  - HCT116 (colon)
  - HepG2 (liver)
  - Or provide your own

- Molecular and cellular assay platforms to interrogate the model of interest
  - Thermo Scientific<sup>™</sup> CellInsight<sup>™</sup> CX7 High-Content
     Screening Platform
  - Thermo Scientific<sup>™</sup> Varioskan<sup>™</sup> LUX multimode microplate reader
  - Applied Biosystems™ QuantStudio™ qPCR platform
- Protocol optimization for your model of interest, with complete transparency to products and methods employed
- Consultation with our experienced custom services research team comprising >150 combined years of cell biology experience



Invitrogen™ LIVE/DEAD™ and Hoechst™ 34580 dye staining of HCT116 spheroids following treatment with staurosporine at (A) 5.5 µM and (B) 0.2 µM. Images were acquired using the Thermo Scientific™ CellInsight™ CX7 HCS Platform in confocal mode with a 10x objective.

## Functional genomics screening—service overview

We can help you identify and validate your target of interest using either our CRISPR or siRNA libraries to interrogate functional pathways, proliferation, gene expression analysis, and protein modifications. Our custom service team can deliver your screening results in 4–6 months.



## Lentiviral CRISPR libraries for functional genomics

### **Target identification**



The next-generation tool for functional genomics screening



Complete, permanent knockout of gene expression



Stronger phenotypes, larger assay window, higher confidence in hits, and clear verification of targets

### 19 libraries

- 17 sublibraries by gene family and functional biology
- Druggable genome
- Whole genome
- Custom gRNA library and Cas9 virus options available

### Invitrogen<sup>™</sup> LentiArray<sup>™</sup> Human CRISPR libraries



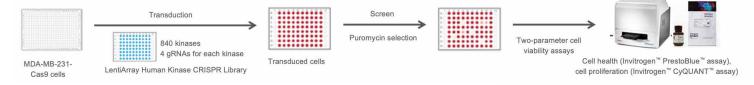
- Available as ready-to-use, high-titer lentivirus or as glycerol stocks
- Organized by gene family and/or function
- 4 gRNAs per gene target per well

### Invitrogen<sup>™</sup> LentiPool<sup>™</sup> CRISPR libraries



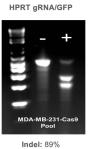
- Delivered as ready-to-use, high-titer lentivirus
- Extensive QC, including NGS, for gRNA representation
- Thousands of gRNAs pooled per tube
- 4 gRNAs per gene target

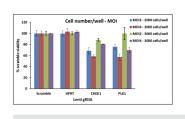
Goal: To identify novel targets in a breast cancer cell line using the Invitrogen™ LentiArray™ Human Kinase CRISPR Library

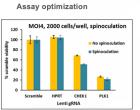


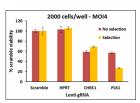
### Generation of a stable Cas9-expressing cell line











Cell seeding: 2,000 cells/well
MOI: 4

Puromycin selection:  $\sqrt{}$ Spinoculation:  $\sqrt{}$  Positive controls: CHEK1 and PLK1

Negative control: Scramble

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

## siRNA libraries for functional genomics screening

Superior siRNAs for *in vitro* RNAi applications are the most effective way to knock down gene expression to study protein function in a wide range of cell types.



## Invitrogen™ *Silencer*™ Select siRNAs have the highest functionality in the industry

- >70% silencing of genes when used at 5 nM concentration
- Proprietary chemical modifications provide highly specific silencing to reduce off-target effects that may cause false positives

### Libraries provide 3 unique siRNAs per gene

- Predefined libraries against popular human gene classes—kinases, phosphatases, GPCRs, etc.
- Customized collections available upon request for all human, mouse, and rat genes
- Researchers can easily rank their hits following a primary screen (3 of 3, 2 of 3, etc.)
- 0.25 nmol siRNA per well

### Lead identification

We offer a wide range of services—from early-stage compound screening to safety and toxicology testing, including SelectScreen Screening and Profiling Services for lead identification.

### **Compound screening**

- Biochemical: kinase profiling
- Cellular: GPCRs, pathways, nuclear receptor profiling

### Selectivity and optimization

- All target classes
- Cell health
- Customer-supplied assays

### Safety and toxicity

- hERG biochemical screening
- P450 biochemical screening
- Cell health

### Why choose SelectScreen services?

- Broad panel of more than 490 purified kinases
- State-of-the-art compound management system

### Why choose SelectScreen services?

Customers have the option to select the full panel, a small subset, or anywhere in between for their screening needs.

- 27,350 projects completed since 2004
- 80% data provided within 48 hours
- 18 million screened since 2004

- 99.6% projects delivered on time
- 3.9-day average turnaround time for biochemical profiling projects

## Lead validation—hERG potassium channels and P450 testing

Overview of safety screening: hERG screening

### hERG screening service overview

- Fluorescent polarization assay, biochemical assay format—Invitrogen™ Predictor™ hERG Fluorescence Polarization Assay (red-shifted)
- Portable assay format—may be brought into client labs for follow-up
- Control inhibitor on every plate
- Offers IC<sub>50</sub> screening service, 10-point titration in duplicate

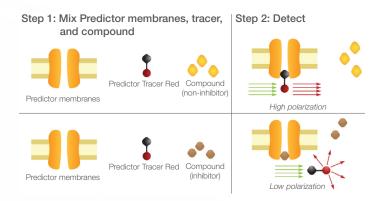
### P450 profiling service overview

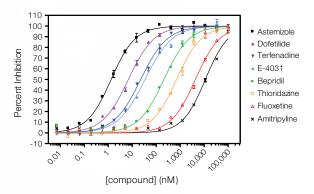
Drug +

Vivid substrate

- Fluorescence intensity, biochemical assay format— Invitrogen™ P450 BACULOSOMES™ and Vivid™ substrates
- Portable assay format—may be brought into client labs for follow-up
- Control inhibitor for each P450 on every plate
- Offers IC<sub>50</sub> screening service, 10-point titration in duplicate

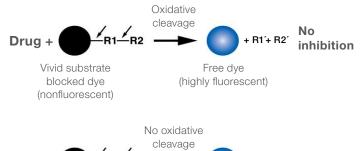
## Predictor hERG assay technology and assay validation

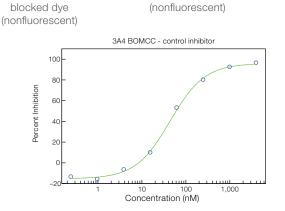




Inhibition with known hERG channel blockers

## P450 Vivid assay technology and assay validation





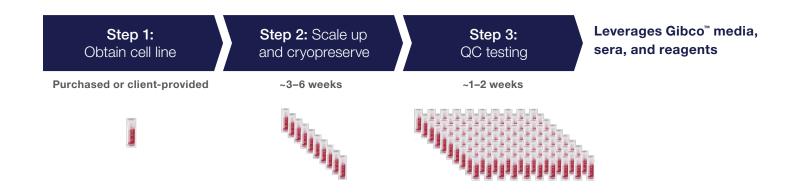
Blocked dye

Ketoconazole inhibitor using CYP3A4 BOMCC assay

+ R1'+ R2' Inhibition

## Overview of bulk screening reagent: cell banking

Get validated, high-throughput functional genomics screening for target identification with our cell banking service in as little as 3-4 weeks.



## Seamlessly integrate with other CellModel and discovery services (assay development, drug screening, etc.)

Leverage established methodology or client-provided protocols and growth conditions

- Standard or engineered cell lines—adherent or suspension
- Primary cell lines
- Stem cells-embryonic, adult
- Any of the prevalidated Thermo Fisher cell lines

## Protein and cell analysis services

Thermo Fisher offers a comprehensive solution for cell and protein characterization, purification, and detection to support your research needs. Take advantage of our broad range of high-quality and cost-effective custom solutions; connect with innovative tools and let our scientists support you on your unique research.

Learn more about our services on the following pages, or reach out to our R&D team for a scientific consultation.

Find out more at thermofisher.com/cellanalysis



## Custom antibody development

Let our team of antibody production scientists help you reach your custom antibody development goals.

We provide the services you need to help you develop a novel polyclonal, monoclonal hybridoma, or recombinant antibody. Thermo Fisher Scientific delivers exceptional antibody development solutions from antigen design to purification and screening.

Immunogen preparation—choose from services including peptide design with a range of peptide modifications, recombinant protein expression, immunogen conjugation, and customer-supplied immunogen

**Antibody production**—choose from recombinant monoclonal and polyclonal, traditional monoclonal and polyclonal, customizable protocols, and additional purification options

**Formulation/packaging**—choose from bulk or custom packaging, special formulation (BSA- or azide-free), custom concentration, and special testing

Antibody conjugation—examples of conjugates include Invitrogen™ Alexa Fluor™ and Thermo Scientific™ DyLight™ dyes, FITC/fluorescein, biotin, HRP, PE, APC, and additional options

Find out more at thermofisher.com/customabs

## Custom peptide synthesis

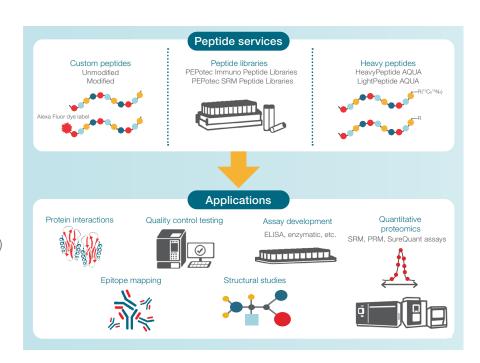
High-quality peptides from a validated process tailored to meet your needs

Our custom peptide synthesis service offers multiple options to meet your needs. We are constantly adapting our product offering based on your input, and our experienced peptide scientists will support you with peptide sequence, scale, and/or purity selections for your assay to help you achieve superior results for your application.

Discovery	Confirmation	Validation
Thousands of peptides	Hundreds of peptides	Tens of peptides
PEPotec SRM peptides (3 gra	ades) HeavyPeptide AC	UA standards (Basic, QuantPro, and Ultimate grade)

#### Custom peptide synthesis capabilities:

- Custom peptides 6–40 amino acids (<6 and up to 105 amino acids also possible)
- Scales from 1 mg to 1 g
- Levels of purity from crude to >98%
- Flexible formatting options
- Extensive list of modifications and labels, including heavy peptides (isotope-labeled)
- Custom conjugation services—e.g., protein—peptide conjugates and multipleantigen peptides (MAPs)



#### Peptide purity recommendations by application

Crude: peptides for high-throughput screening
>70%: antigens for polyclonal antibody production
>75%: ligands for affinity purification, enzyme substrate studies, epitope mapping
>80%: qualitative peptide blocking studies, protein electrophoresis applications
>85%: immunological applications, peptide arrays, affinity purification
>90%: qualitative bioassays, monoclonal antibody production
>95%: quantitative bioassays (e.g., ELISA, enzymology, biological activity)
>97%: MS proteomics applications
>98%: structural studies, crystallography, NMR, in vivo applications

Note: Listed purity levels indicate the minimum typical requirements for each application.

	Standard peptides	PEPotec® Immuno Custom Peptide Libraries Peptide Libraries Peptide Libraries		HeavyPeptide <sup>™</sup> and LightPeptide <sup>™</sup> AQUA standards  Quantitative mass spectrometry	
Primary application	blication Basic research or biomarker discovery Epitope mapping, vaccine development		Discovery		
Key features	Over 400 modifications available	High throughput, low toxicity	High throughput	High quality and accurate concentration	
Peptide length*	2-110 amino acids	6-20 amino acids	6-25 amino acids	Up to 15 amino acids	
Manufacturing scale**	1 mg-1 g	≥1 mg	≥0.1 mg	Multiple scales available	
Purity	Crude (>50%) to >98%	Crude (as synthesized)	Crude (as synthesized) or >70%	>95%	
Quality control	MALDI-TOF MS and HPLC	MALDI-TOF MS	MALDI-TOF MS check or analysis; HPLC for purified grade	MALDI-TOF MS, HPLC, AAA	
Production time	2-3 weeks	4 weeks	2–3 weeks 2–3 weeks for AQUA Express 5–7 weeks for standard AQUA		

<sup>\*</sup> Please inquire about longer peptide lengths.

## Find out more at thermofisher.com/peptides

<sup>\*\*</sup> Greater amounts available upon request.

## Standard peptides

- High quality—all peptides are synthesized with highquality materials
- Modifications—most comprehensive list of available modifications and labels
- Validated—all peptides are analyzed by MS alone or in combination with analytical HPLC
- Flexible—peptides available in a variety of formats and purities; manual synthesis available for difficult peptides

Specifications for standard-grade peptides Peptide length\* 2-110 amino acids. L- or D-isoforms Manufacturing scale\*\* 1 mg-1 g Crude (>50%) to >98% pure Purity Counterion TFA Formulation Lyophilized **Delivery format** Glass vial Production time Standard delivery within 2-3 weeks Shipment Lyophilized at room temperature MALDI-TOF MS for crude peptides: MALDI-TOF MS and HPLC for all Quality control other purity grades Extensive list of modifications and Modifications labels, including heavy peptides (isotope-labeled) Custom conjugation available, Conjugation e.g., protein-peptide conjugates and multiple antigen peptides (MAPs) Alternate counterion, amino Optional services acid analysis, endotoxin testing, solubility testing

We offer a wide range of N-terminal, C-terminal, and other modifications with our standard peptide service. Please go to **thermofisher.com/peptides** for the most up-to-date list and available positions in the peptide sequence.

Custom conjugation services are also available, including conjugation to carrier proteins (KLH, BSA, OVA, or Thermo Scientific™ Imject™ Blue Carrier™ Protein) and MAPs.

## Peptide modifications offered with standard peptide synthesis

- Acetylation of N terminus (Ac-NH-)
- Acetyl-lysine
- Aldehyde
- Alexa Fluor dyes
- 6-amino hexanoic acid (Ahx)
- 6-amino caproic acid (Aca)
- Amidation of C terminus (-CONH<sub>2</sub>)
- Amino benzoic acid
- Beta-alanine
- Biotin
- Carbamidomethylation
- Citrulline
- Conjugation to proteins (BSA, KLH)
- Conjugation to oligonucleotides
- Custom FRET peptides
- Cyclization via termini or disulfide bridge
- D-amino acids
- Dabcvl
- Dabsvl
- Dansyl
- Dihydroxy tyrosine
- Dimethyl lysine
- Dinitrophenyl (DNP)
- EDANS

- Farnesyl
- Fluorescein (FITC/5-FAM)
- Hydrocarbon spacers
- Hydroxy proline
- Hydroxy tryptophan
- Isotopically labeled amino acids (with <sup>13</sup>C, <sup>15</sup>N)
- Mercaptopropionic acid
- Methoxy coumarin acetic acid (MCA)
- Methionine sulfone
- Methionine sulfoxide
- Monomethyl lysine
- Monomethyl arginine
- Multiple-antigen peptides (MAPs)
- Norleucine (NIe)
- Polyethylene glycol (PEG) spacer
- Pyroglutamic acid (Pyr)
- Rhodamine B
- Rhodamine 110
- Special amino acids (D-amino acids, other amino acids)
- Tetramethylrhodamine (TAMRA)
- Invitrogen<sup>™</sup> Texas Red<sup>™</sup> dye
- Ubiquitination
- Other dyes or modifications on request

<sup>\*</sup> Please inquire about longer peptide lengths.

<sup>\*\*</sup>Greater amounts available upon request.

## PEPotec peptide libraries

#### Thermo Scientific™ PEPotec™ Immuno Custom Peptide Libraries

Fully synthetic custom libraries that support highthroughput screening assays to map epitopes or identify immunogenic sites in proteins

## Thermo Scientific™ PEPotec™ SRM Custom Peptide Libraries

Fully synthetic, crude peptides customized for the development of medium- to high-throughput SRM and MRM assays

		PEPotec immuno pe	ptide library service	•		
	PEPotec Immuno Custom Peptide Libraries	PEPotec SRM Custom Peptide Libraries				
		Grade 1	Grade 2	Grade 3	HPLC >70% pure	
		Fast and easy	Greater analysis	Maximum assurance	Guaranteed purity	
Peptide length*	6-20 amino acids; L-isoforms only	6-25 amino acids				
Quantity	≥1 mg		≥0.	1 mg		
Purity	Crude (as synthesized)**	Crude (as synthesized) >70% (guarante				
C-terminal residue <sup>†</sup>	Any unmodified L-isoform amino acid	Lysine (K) or arginine (R)				
Counterion	Acetate		Т	FA		
Formulation	Lyophilized	Suspended in 0.1% TFA in 50% (v/v) acetonitrile/water				
Delivery format	Peptides pro	ovided in individual 2D barcoded tubes in Thermo Scientific™ Matrix™ 96-tube plates				
Production time	4 weeks	2–3 weeks				
Shipment	Lyophilized at room temperature	In solution on wet ice				
Minimum order	4 peptides; surcharge for orders of <48 peptides	24 peptides; surcharge for orders of <48 peptides	rs of 4 peptides; surcharge for orders of <48 peptides			
Quality control	MALDI-TOF MS <sup>‡</sup>	MALDI-TOF MS analysis of 5% of peptides	MALINE MS analysis		MALDI-TOF MS and HPLC analysis of 100% of peptides	
Included documentation	Peptide amount	Peptide amount		Peptide amount and MS spectra	Peptide amount, MS spectra, HPLC	
Peptide resynthesis	Not provided	Not provided		One resynthe	One resynthesis provided	
Failed synthesis policy	Not provided	You pay for entire set of peptides ordered	You only pay for peptides successfully synthesized in the requested library			
Modifications	Lys acetylation Cys carbamidomethylation Phosphorylation, etc.	Single or double phosphorylation (pY, pT, or pS) Cysteine carbamidomethylation (CAM) Methionine oxidation [Met(O)] Internal heavy amino acids Alternative heavy amino acid at the C terminus Other modifications available on request				
Optional services	Solubilization in DMSO, individual tube labeling, etc.	Lyophilization, individual tube labeling				

 $<sup>^{\</sup>star}$  Please inquire about longer peptide lengths and manufacturing scale.

<sup>\*\*</sup> No purification given, as peptide purity is sequence-dependent and a function of different liquid chromatographic conditions.

<sup>†</sup> Other stable isotope-labeled amino acids are available; please inquire.

<sup>‡</sup> For all peptides except phosphopeptides, the three major peaks in the MS analysis represent the target of interest. Peptides must pass both the MS analysis and the final gross weight criteria (>1 mg) before shipment. If peptides do not pass these criteria, the customer will be informed and one resynthesis will be offered free of charge.

## HeavyPeptide and LightPeptide AQUA standards

High-quality isotopically labeled peptides for absolute quantitation

The Thermo Scientific™ HeavyPeptide™ and LightPeptide™ AQUA Custom Synthesis Services provide isotopically labeled or unlabeled AQUA (Absolute QUAntitation) peptides with extensive QC for the relative and absolute quantitation of proteins by mass spectrometry.

#### Highlights

- Precise—peptide concentration guaranteed from AAA
- Sensitive—enables absolute quantification of low-abundance (fmol) proteins
- Specific—100% peptide sequence specificity
- Flexible—variety of purity, modification, and formatting options



Specifications of HeavyPeptide and LightPeptide AQUA standards						
	AQUA Ultimate	AQUA QuantPro	AQUA Basic			
Research stage	Validation or clinical, ideal for absolute quantitation	Confirmation or validation, ideal for biomarker verification	Discovery, confirmation or validation, relative quantitation			
Peptide length*	Up to 15 amino acids					
Amount/aliquot number	10 nmol/- 40 nmol/- 96 nmol/s	15 to 30 nmol (0.05 to 0.1 mg)/1 aliquot				
Purity	>9	>95%				
Isotopic enrichment	>99%					
Standard (light) peptides available	Yes					
Formulation	5 pmol/µL in 5% (v	Lyophilized				
Delivery format	Glass vial					
Production time	5–7 weeks standard AQUA 2–3 weeks AQUA Express					
Shipment	In solution	Dry at room temperature				
Quality control	MALDI-TOF MS, HPLC, quantitative AAA					
Concentration precision	±5-10%	±10-25%	NA			
Modifications	Single or double phosphorylation (pY, pT, or pS) Cysteine carbamidomethylation (CAM) Methionine oxidation [Met(O)]					
Optional services	Other modifications available on request					

<sup>\*</sup> Please inquire about longer peptide lengths.

## Immunoassay custom services

Our immunoassay R&D team has over 30 years of experience with immunoassay development, sample handling, data analysis, and project management to deliver solutions to significantly shorten your path from sample to discovery.

Not sure where to start? We offer valuable consultation services, free of charge.



Custom immunoassay development



Service lab (e.g., sample measurement)

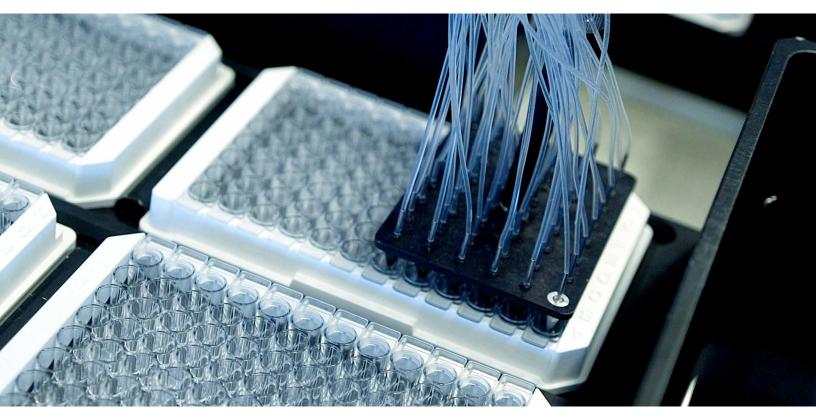


Lot reservation and bulk packaging



Manufacturing services (e.g., coupling with alternative antibodies)

Find out more at thermofisher.com/immunoassayrequests



## Immunoassay development

Operating in an ISO 9001—certified facility with high-quality standards and procedures, our specialized research group develops custom products according to your project needs.

#### Custom assay services include:

- Dedicated project manager
- Initial R&D scientific consultation
- Regular project updates
- Confidentiality of your data

- Milestone plan in three phases
  - Phase 1: Feasibility (antibody pairing)
  - Phase 2: Development (and optimization)
  - Phase 3: Validation (reproducibility, stability)

## Lot reservation and bulk packaging

#### Lot reservation

Request multiple kits from a single lot for large or long-term studies from the Invitrogen™ immunoassay portfolio

#### **Bulk packaging**

- Obtain products in bulk packaging for less waste, better use of storage space, or high-throughput automation needs
- Request additional components or special formulation



Coated ELISA



Validated, gold-standard ready-to-use ELISA kits



ProQuantum kits



2–5 µL sample concentration, high-sensitivity protein detection on qPCR instruments





Measure multiple proteins simultaneously in one well (up to 80 proteins) on Luminex<sup>™</sup> systems

#### Additional operational services:

- Plate coating—96-well clear, white, or black
- Filling vials
- Custom lyophilization

Please inquire for more details on thermofisher.com/immunoassayrequests

## Gene expression analysis service

Outsource and accelerate your gene expression research with the Invitrogen™ QuantiGene™ Plex assay service and our in-house scientists in Madison, WI. Our assay service is designed to help you meet your specific project goals and timelines so you can free up valuable resources for other discovery research.

#### Assay services features and benefits:

**Design support**—save time by accessing our bioinformatics team to customize your probe and panel design; obtain high-quality data with fast turnaround times; assay measures up to 80 transcripts/RNA targets per well

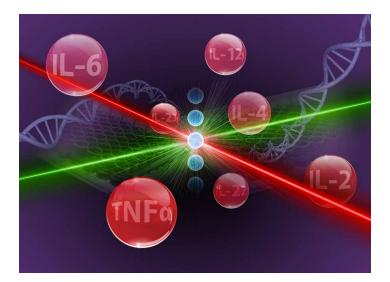
**Consistency**—use the same customized assays in your follow-up studies that our team uses in the service

**Flexibility**—sample types include purified RNA, cultured cells, or tissue (whole blood, fresh or frozen tissue, or formalin-fixed, paraffin-embedded (FFPE)) pre-lysed in Invitrogen™ QuantiGene™ Buffer

**Choice**—a comprehensive list of target areas, including immunology, inflammation, cancer signaling, toxicology, neurology, cardiology, bone biology, metabolism, endocrinology, stem cell biology, apoptosis, and autophagy

Sample types accepted (our experienced professionals provide support and instructions for your specific sample prep needs):

- Cell lysates
- Whole blood lysates
- Tissue and FFPE tissue homogenates
- Purified RNA



## GeneArt DNA and protein services

# Your partner for DNA synthesis all the way through to protein production

Since being founded in 2000, GeneArt services have been at the forefront of many synthetic biology applications by democratizing access to DNA—the building blocks of life—to enable scientists to put research concepts directly into biological code. The synthesis of DNA is the driving force behind new and emerging synthetic biology technologies, including those used in the fight against infectious diseases and pandemics. GeneArt technology offers a comprehensive set of tools and solutions to accelerate discovery.

Find out more at thermofisher.com/geneart



## Gene optimization

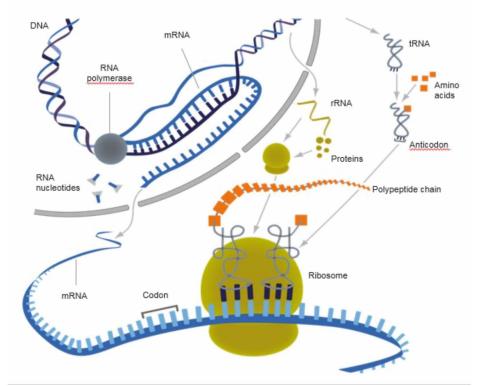
## Maximizing protein expression at no additional cost

Protein expression involves several key steps and high levels of expression can often be difficult to achieve. Gene optimization is the solution to the limitations of traditional protein expression. Common pain points associated with protein expression, such as yield, can now be addressed in a rational and systematic way. Using data available from published literature in combination with proprietary data, the GeneOptimizer algorithm determines the optimal gene

sequence for your expression experiments.

## GeneArt GeneOptimizer sequence processing:

- Identifies the best way to incorporate your requested sequence elements
- Eliminates cryptic splice sites and mRNA-destabilizing sequence elements for increased mRNA stability
- Optimizes codon usage and adapts GC content to your expression system
- Avoids undesirable mRNA secondary structures
- Eliminates repetitive sequences
- Includes siRNA-resistant forms of wild type genes that can be used in RNAi



Many providers of synthetic genes offer some form of gene optimization but quite often these are limited to just codon optimization with a few additional parameters. Our GeneOptimizer algorithm enables true multiparametric optimization, dealing with a large number of sequence-related parameters involved in different aspects of gene expression, such as transcription, splicing, translation, and mRNA degradation.

## GeneArt Gene Synthesis

## High-quality, 100% accurate cloned genes

GeneArt Gene Synthesis services offer ease, flexibility, and reliability for your daily DNA work. Gene synthesis is a cost-effective, time- and resource- saving method for obtaining your desired DNA construct with 100% accuracy. It is a true alternative to conventional molecular biology techniques, while enabling better, more reliable protein expression and quality. GeneArt Gene Synthesis tools go beyond traditional gene synthesis by enabling expression optimization for maximum performance.

Invitrogen

Structure de la company de la co

- Industry-leading optimization—with proprietary Invitrogen™ GeneArt™ GeneOptimizer™ software, you can realize substantial gains in protein expression levels compared to wild type sequences, at no extra cost
- Easy and intuitive online ordering using GeneArt<sup>™</sup> Instant Designer
- Nearly unlimited flexibility in gene and vector design
- Ready-to-use constructs for expression and transfection
- Maximum production speed and worldwide delivery; capacity and reliability supported by a fully automated, industrial-scale gene processing platform

#### GeneArt Gene Synthesis





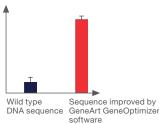
GeneOptimizer optimization algorithm
GeneAssembler gene synthesis platform











#### **Classic cloning**

cDNA library

PCR amplification

Addition of cloning sites

Ligation and transformation

Colony screening

Sequencing

Plasmid with natural gene





















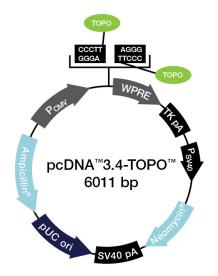


GeneArt Gene Synthesis and optimization are faster than classic cloning methods and can provide better results.

Find out more at thermofisher.com/genesynthesis

## GeneArt cloning and plasmid DNA purification services

Choosing a vector for the delivery of your gene



Once we synthesize your gene *de novo*, we offer several vector options designed to provide you with maximum flexibility and speed of delivery.

I'm looking for:	My chosen synthesized gene in a basic vector	A vector for protein expression	A wide range of vectors to choose from	Personalization with the option to use my own vector
Options	Options  Have your selected gene delivered in our standard Thermo Scientific GeneArt pMX shuttle vector.  Get clon selected gene detailed.		Use one of our available Invitrogen™ vectors, or purchase a specific vector for us to clone the selected gene into.	Send us your own vector and we'll clone the <i>de novo</i> synthesized gene into it.

Note: We do not perform any kind of cloning services unless we synthesize the gene de novo.

#### GeneArt plasmid DNA purification service

The Invitrogen™ GeneArt™ plasmid service can prepare research-grade plasmid DNA (pDNA) and preclinical-grade pDNA with quality-controlled systems and reagents using proven protocols. GeneArt facilities are ISO 9001:2015–certified and consistently provide products and services that promote customer satisfaction and regulatory compliance. Preclinical-grade pDNA comes with outstanding quality control and documentation as requested. GMP-scale plasmid preparation services are also available. Endotoxin and bioburden testing is also available for plasmid prep yields over 1 mg. For more information, visit thermofisher.com/patheon



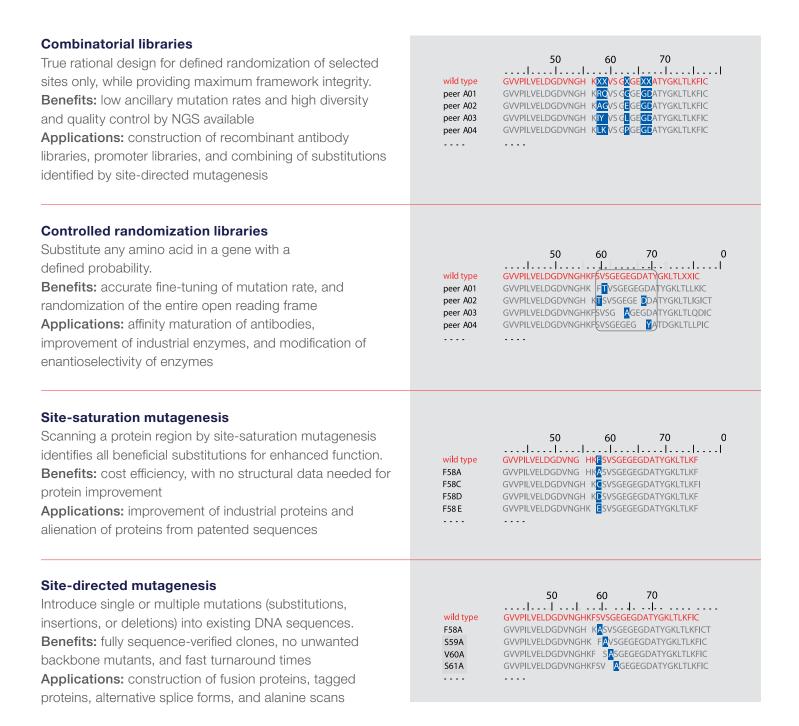


Our highly pure, homogeneous plasmid DNA is ready for transfection and transformation:

- Extremely low endotoxin levels (<0.1 EU/µg pDNA at selected scales); generally considered endotoxin-free
- Microgram- to milligram-scale production
- Flexible delivery options—liquid or frozen on dry ice
- Fill-and-finish service available—get pDNA in labeled aliquots for immediate use per your specifications

## Creating improved proteins

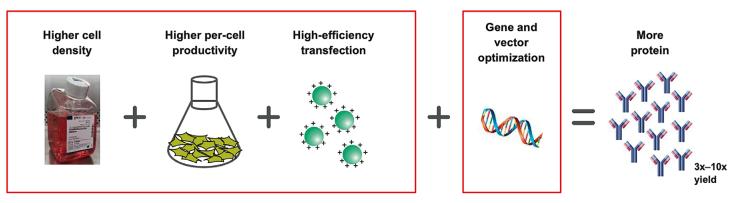
#### GeneArt Directed Evolution



## GeneArt protein expression and purification services

Partner with us to expedite antibody and drug development discovery

Our GeneArt protein expression and purification services offer a rapid and dependable way to obtain correctly folded native protein from transiently transfected mammalian or insect cells. GeneArt services have more than 20 years of experience in the bioproduction of genes and transient proteins, and our integrated bioproduction services will expedite the discovery process from pilot through to commercial scale.



GeneArt Gene Synthesis with advanced Gibco™ expression systems can increase transient protein yields.

Find out more at thermofisher.com/genetoprotein

#### Advantages of using Gibco™ Expi293™ or ExpiCHO™ system:

- Available in both mammalian (HEK293, CHO-S) and insect (Sf9) cell line formats
- Up to 20x more protein in less volume
- Expression yields up to 3 g/L
- Scalable expression from <1 mL to >10 mL
- 5–14 days for rapid protein production
- Fully documented cGMP offerings

We also offer expression via our Gibco™ ExpiSf™ Expression System. For more information, go to **thermofisher.com/expi** 



# High-throughput (HTP) ExpiCHO expression and purification

The Invitrogen™ GeneArt™ HTP ExpiCHO Expression Service offers cost-effective, small-scale options to rapidly analyze variant constructs to support acceleration of antibody discovery. We offer a 24-well and a 96-well format and delivery in as little as 21 days starting with *de novo* gene synthesis.

Size	Culture volume	Samples per plate	Controls per plate*	Quantity after purification	Final volume	Control minimum
24-well	2.5 mL	20	4	10 μg-1.8 mg	350 µL	200 µg
96-well	0.8 mL	92	4	1-500 µg	150 µL	75 µg

<sup>\*</sup> Controls are included on each place across the plate (+ rlgG, - mock). Mock wells can be replaced by specific controls requested by the customer.

#### Find out more at thermofisher.com/g2pservice



# Gene synthesis customer care provides exceptional support



#### Information is the key

We recognize that seamless information flow is a crucial part of your project design and execution. Both the ability to consult us for individual questions and the broad archive of educational information available on our website create a superior knowledgebase supporting your research.



#### **Optimal fit**

Wherever your research is starting, we can tailor the supply material for your genes in a manner compatible with your entire research workflow, from gene to protein.



#### **Excellence through connection**

The GeneArt Gene Synthesis Customer Care Group is connected to you via your local technical support specialist (TSS) or account manager, and to your gene project via the manufacturing, logistics, and R&D groups. We have all the resources to provide holistic project care from initial idea to final delivery.



#### **High-capacity capabilities**

We service over 1,750 customers on over 7,600 gene constructs each month, so you can be sure we have the global capacity to meet your research needs.



#### **Customer always first**

Your GeneArt Gene Synthesis Customer Care Group is a team of scientists and specialists based in Europe and the US who are always eager to provide the best technical and customer service.



#### Global sales support

For excellent support in multiple languages and time zones, the GeneArt Gene Synthesis Customer Care Group is supported in the field by 35 technical sales specialists located around the world, committed to assisting you.



#### Global technical support

In addition, more than 200 TSSs located at 18 sites around the globe provide in-depth assistance via email, phone, or chat in 11 different languages to nearly one million customer contacts per year. Our global TSS team has won the Life Science Industry Awards for several years.

## Our commitment to you and the environment

#### Sustainability matters to us

At Thermo Fisher, we take responsibility for our environmental impact. Every year, more and more waste is generated by humans. Greater self-awareness on the part of consumers is encouraging, but individuals are only part of a complex waste-reduction equation. Businesses must take stock, too. We have 16 externally certified zero-waste sites around the world as of 2021, including our Regensburg (Germany) production site for GeneArt projects.

#### It's paper. It's cool.

Some of our biggest environmental impact has been due to cold shipping. Traditional expanded polystyrene (EPS) foam coolers are good for protecting products but are difficult to recycle, which creates disposal issues for our customers. Our 100% paper cooler is an environmentally preferable alternative to EPS coolers, and it upholds the thermal requirements necessary for products to meet our stringent quality standards.



#### Here are some examples of how we've reduced waste

#### Redesigned GeneArt product packaging

- We replaced the original 20-tube rack with an 8-tube rack for a 54% reduction in weight and a 1,100 kg reduction of cardboard
- We use fully recyclable cardboard
- The redesigned packaging improves functionality for our customers



#### Developed an automated reagent transfer system for oligo synthesis

- Makes manual handling of hazardous substances unnecessary
- Reduces labor time
- Reduces glass waste by approximately 20 tons per year and cardboard waste by 4.5 tons per year
- Reduces reagent and waste disposal costs



## Enabled data transfer for quality assurance documentation (QAD) via the Thermo Fisher™ Connect Platform

- Download QAD from Connect Platform instead of receiving a CD with your shipment—look for the GQ icon
- Eliminates printed manuals and product information and the need to store QAD on CDs





## Case study

GeneArt protein purification services, with ExpiCHO Expression System

Utilizing strategic outsourcing with our GeneArt purification services, you can deliver 50% more proteins and antibodies, and save >2,000 FTE hours/year.

#### **Situation**

- A privately held biotechnology company explores numerous new and novel proteins and antibodies to test on their immunotherapy platform to fight various diseases including cancer.
- Using the Expi293 Expression
   System for expression and
   purification of their proteins and
   antibodies of interest, they were
   looking to increase productivity.
   Overall, the aim was to:
  - Increase protein and antibody production
  - Reduce FTE hours required

#### **Our response**

- Introduced ExpiCHO mammalian expression system. The system delivered higher yield; however, many FTE hours were still required to perform expression and purification of targets in house.
- Introduced GeneArt protein purification services with proprietary GeneArt GeneOptimizer technology to help save time and resources for producing relevant protein and antibody targets.

#### Value delivered

- Customer achieved productivity gains leading to faster turnaround on data, resulting in identification of additional targets for screening and securing of private funding.
  - Approximately 50% more proteins and antibodies delivered through outsourcing the production of 90% of their proteins
  - Saved >2,000 FTE hours/year (equivalent of one FTE;
     40 hours/week x 52)

## Bioproduction

## Driving performance through collaboration

#### **Expression plasmid**

- GeneOptimizer algorithm increases yield
- Full design flexibility
- Invitrogen vector suite
- High-quality plasmid preparation
- Gene-to-protein inhouse process provides full control

#### **Expression**

- Flexible expression scales
- Parallel workflows for high throughput
- Expi293 and ExpiCHO expression systems
- Bac-to-Bac system with Sf9 cells

#### **Purification**

- Multiple parallel purifications
- Crossflow filtration system
- Fast pre-purification titer detection system
- Capacity of >5,000 antibody purifications/year
- >500 non-antibody purifications/year

#### Analysis

#### Standard:

- SDS-PAGE or western blot
- Thermo Scientific<sup>™</sup>
   NanoDrop<sup>™</sup>
   spectrophotometer
- Capillary gel electrophoresis (LabChip™ CX2 system, Caliper™)
- Analytical size exclusion chromatography (HPLC)
- Endotoxin detection

## Translational research

Thermo Fisher Scientific is committed to advancing translational research, supplying the highest-performance solutions for custom media, sample handling, and cell and gene therapy solutions. Along with our innovative solutions to difficult research challenges, we partner with key thought leaders to bring you the most current approaches and breakthroughs in this field.



## Cell and gene therapy

## Overview of cell therapy services



#### **Collection and tracking**

• Cold-chain supply logistics



#### Cell isolation and engineering

• Lentiviral production system



#### Cell therapy manufacturing services

- Process development
- QC and analytical assay development
- cGMP manufacturing



## Characterization, lot release, and preservation

- Cell line authentication
- Potency assays



#### Formulation, supply chain, and logistics

- Cryopreservation
- Cold-chain supply logistics
- Clinical trial support

Learn more at thermofisher.com/celltherapy

## Overview of gene therapy services



#### **Vector construction**

- Gene synthesis
- GMP plasmid production





#### Characterization and lot release

- Identity, purity, and contamination
- Functional titer
- Analysis of empty capsids
- Genomic, proteomic, and cellular analytical tools



#### **Vector production**

Custom media



#### **Vector purification**

- Affinity chromatography
- Ion-exchange chromatography
- Centrifugation



## Viral vector manufacturing and commercialization services

- Process and method development and optimization
- Cell line development
- Master cell banking
- Viral vector assembly
- Scale-up to GMP for clinical or commercial manufacturing
- Sterile fill/finish of viral vector



#### Formulation, supply chain, and logistics

- Aseptic fill/finish
- Cryopreservation
- Cold-chain supply logistics
- Clinical trial support
- Global distribution



# Overview of viral vector manufacturing and commercialization services

Unparalleled experience and track record for manufacturing viral vector products for over 20 years

#### **Experience**

- Manufacturing of cGMP clinical and commercial lots for >500 viral vectors
- >100 viral vector products made
- Commercial-use license obtained and being expanded

#### **Technical expertise**

- >1,000 experienced colleagues worldwide
- Analytical and process development
- Process characterization and validation
- Technology transfer
- Regulatory compliance

#### Capacities and capabilities

- 650,000 ft<sup>2</sup> capacity available today
- 45 drug substance suites
- 8 drug product suites
- · Regulatory services
- Fill/finish services for viral vectors
- Supply chain and commercial packaging solutions



## Process and analytical development

Alachua, FL 95,000 ft<sup>2</sup> Lab/GMP warehouse development; clinical



#### Clinical supply

Cambridge, MA 140,000 ft<sup>2</sup> Manufacturing site and HQ; clinical and commercial



## Characterization and validation

Lexington, MA 64,000 ft<sup>2</sup> Manufacturing site; clinical and commercial



#### Commercial launch

Plainville, MA 290,000 ft<sup>2</sup> Manufacturing site; clinical and commercial

Learn more at thermofisher.com/viralvectors

## End-to-end solutions to support cell and gene therapy manufacturing and commercialization



#### **GMP** plasmid manufacturing

- Process development and optimization
- Master cell banking
- Scale-up to GMP for clinical and commercial manufacturing
- Critical raw material or drug substance
- In-process and release testing
- Stability testing and storage



#### Viral and cell cloning and banking

- Molecular biology
- Virus and cell cloning and screening
- cGMP virus and cell banking
- HEK and Sf9 cell lines available for use



#### **Process development**

- Suspension and platform processes
- Process transfer, development, and optimization
  - Cell culture
  - Transfection and infection
  - Purification
- DOE and process characterization



#### Analytical development and QC

- Viral vector platform assays
- Assay development, qualification, and validation
- QC release and stability testing
- Assay bridging studies



#### cGMP bulk manufacturing

- Suspension and adherent modalities
- Clinical and commercial-scale capacity
- Operational excellence and rightfirst-time metrics



#### Formulation and cGMP fill/finish

- Formulation evaluation
- Semi-automated and automated filling
- Prequalified vial/container closures
- Primary vial labeling and packaging



#### Clinical trial and cold-chain logistics

- Specimen collection, cold-chain logistics, and cryogenic storage
- Clinical packaging, labeling, and distribution
- Qualified shipping solutions and specialty courier services

### Custom media

Collaborate with the Gibco™ PD Express Services team for all your upstream media needs. We understand the importance of transparency and having products developed specifically for your unique program. This is why with Gibco PD Express Services, it's not just about what we do, but how we do it.

#### Level of our involvement and key services

## Customer owns and develops

Making your medium

# Catalog product evaluation







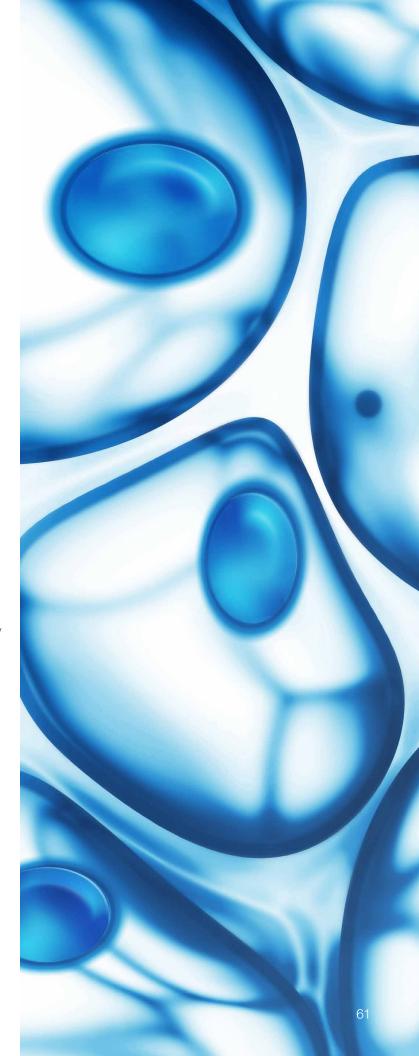


**Customer outsources** 



- 1. Making your medium: When you have your own developed formulation, we can help troubleshoot processes or provide your formulation in any of our several formats (e.g., liquid, liquid concentrate, standard dry powder (DPM), and Gibco™ Advanced Granulation Technology™ (AGT™) so that you can have consistent, high-quality raw materials to go into your process.
- 2. Catalog product evaluation: Accelerated timelines, higher titer requirements, and an increasing number of catalog options demand a well-planned approach to cell culture development. We can help by analyzing your unique production requirements and providing you with cell culture options. The combination of catalog options that we provide is optimized to help you save time, effort, and cost.

- 3. Gibco™ Rapid Prototyping Services: Gain confidence with our reliable, nimble, and responsive non-GMP custom service. Gibco Rapid Prototyping Services are the ideal solution for:
  - Small-scale process development for bioprocessing (ability to tweak formulations)
  - Testing of newer formats for equivalency to original formulations for better efficiencies in scale-up
- 4. Bioproduction analytics: We help process development scientists optimize their cell culture systems by analyzing media components as well as performing stability studies. We analyze spent media to measure amino acid and water-soluble vitamin levels, as well as other components, to identify potential improvements to your formulation and to address the nutrient needs in your unique cell culture system.
- 5. Media and feed panel options: Our media and feed panel evaluations provide rapid access to diverse libraries. Allow our experienced scientists to help identify optimal media for target clones, so that you can obtain improved productivity and titers.
- 6. Media development: Projects can be completed at your facility or ours to specifically achieve your media development goals. Flexible media development options include our new multi-omics workflow as well as a traditional workflow.
- 7. Cell line development: Gibco™ Freedom™ kits provide beginning-to-end stable cell line development options to simplify your workflow and accelerate your processes to commercial manufacturing. All Freedom cell line development kits contain cGMP-compliant products, with no need to source components or develop vectors, plus flexible commercial licensing choices.



## Custom projects

With our wide range of proprietary products, solutions, equipment, and custom project offerings coupled with our highly trained staff scientists, we can help you meet even your most challenging research goals. From 3D organoid generation to protein expression, from cell culture media and assay development to screening and profiling, or from biomolecule labeling to custom packaging, we can provide custom solutions to meet your research needs.

Find out more about how we can partner together at **thermofisher.com/custombiology** 



## Custom outsourced services

When your work requires specialized, reliable, high-quality solutions, count on our team of experienced professionals to help ensure the best workflow options for your research goals. Our wide range of service capabilities leverages a diverse portfolio of quality and consistency, built by some of the most recognized life science brands in the industry.

We have a passion for science and want to see you succeed in every aspect of your research.

Don't see a service you need, or have a complex problem? Reach out to us and discuss it with our R&D team.

Find out more at thermofisher.com/customservices





