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CliniSciences

INTRODUCTION

Clinisciences Group provides a comprehensive range of scientific services to support the research and development needs of the life sciences industry. Our mission is to empower researchers and healthcare professionals with the tools and expertise they need to advance their work and improve patient outcomes. Our services cover a broad range of areas, including:



Simple linear peptides
Complex peptides; cyclic,
Long chain peptides (up to 112 amino acids)
Modified amino acid containing peptides
Various grades of purity: crude, desalted, >75%,
>85%, >90%, >95%, >98%.

Protein production and purification in prokaryotic systems Protein production and purification in eukaryotic systems Cell-Free Protein Expression Expression of Difficult Proteins: Challenges and Solutions

Protein Production





Production of monoclonal antibodies Polyclonal Antibody Production Bispecific Antibody Production Antibody Modification Antibody sequencing

Design-Protein on Demand Purification-High Purity Protein Synthesis-Automated Synthesis Folding-Maximizing biological activity

Chemical Synthesis





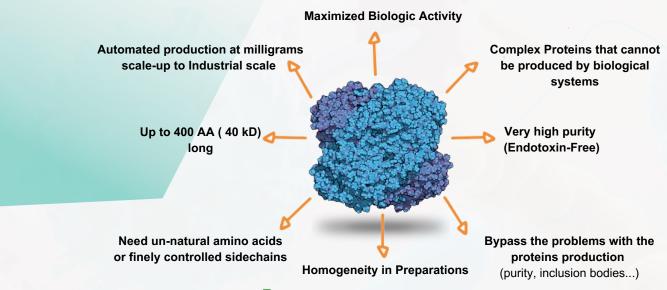
Protein activity
Aggregation status
Protein stability
Protein mass (HPLC-CHIP/QTOF)

CHEMICAL SYNTHESIS OF BIOLOGICS (PEPTIDES, PROTEINS AND ANTIBODIES)



THERAPEUTIC, VACCINE, ANTIGENIC AND DIAGNOSTIC PROTEINS

- Our core focus lies in the design and production of therapeutic proteins (R&D and GMP) tailored for pharmaceutical and biotechnological collaborators. Employing an automated process, we excel in the manufacturing of complexe and highly personalized proteins, reaching up to 400 amino acids.
- Our mission: Develop and accelerate your projects for the production of therapeutic proteins and vaccines.
- Our vision: Enhance the purity and safety of today's and tomorrow's biopharmaceutical products.



Our service

We master the protein synthesis process, making specific modifications to meet your most demanding needs. Protein creation is a true collaboration. We work hand in hand to design, customize, and optimize your proteins to best suit your requirements

Design - Protein on Demand

We design the desired protein (fusion, cyclic, post-translational modifications, or specific modifications).



3 Purification - High Purity

We don't need to perform multiple purifications to achieve high purity

Protein Synthesis -Automated Synthesis We synthesize the protein amino acid by amino acid using our innovative and automated technology

4 Folding - Maximizing Biological Activity

If necessary, we fold the protein to ensure its biological activity

Partners and customers







BIOTECH



INSTITUTES & FOUNDATIONS



ACADEMIC RESEARCH

Our Values



EXPERTISE

Our expertise in protein accumulated synthesis, over more than 20 years, enables us to meet the challenges of designing producing your therapeutic proteins.



RELIABILITY

For more than a decade we have been dedicated to successfully executing all entrusted projects.



RESPONSIVENESS

In pharmaceutical projects, changes are frequent, and some can't be anticipated. We adapt to your needs and any changes you encounter.



CLIENT FIRST

We listen to your needs build therapeutic proteins together that enhance human health.

Our commitments

Innovation:

Expertise, innovation, and customer satisfaction are our priorities. To achieve this, our R&D service works daily to enhance our production processes and introduce new products and services.

Our R&D team, composed of researchers and scientists, optimizes and develops manufacturing processes to address specific challenges related to your proteins (solubility, purity, or functionality).



Optimizing Your Proteins:

Through its expertise and exclusive technological platform, we design and optimize molecular structures with the aim of making them:

• Purer • More Stable • More Soluble • Biologically More Active • ...and more.

Customized Production of Therapeutic Proteins:

Our platform is designed to produce proteins at every stage of development, from research to clinical batch production (GMP).

Using automated production methods, we ensure an easy and efficient transition to the industrial stage, including:

- · Assembly of proteins amino acid by amino acid
- Complete mastery of the production process
- · Reproducibility of processes

Please contact us at tech@clinisciences.com for more information or for a quote request.

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PEPTIDE SYNTHESIS



Peptides are used for a wide range of applications, from polyclonal antibody production to development of therapeutic molecules

Our Custom Peptide Production Services

Our extensive experience in peptide synthesis technologies has afforded us the capability to take on a wide range of sequences, purity levels, and modifications to meet your research needs.

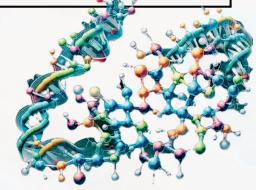
Peptide synthesis typically involves coupling the carboxyl group of an incoming amino acid to the N-terminus of the growing peptide chain, following a C-to-N direction. This approach contrasts with protein biosynthesis, where amino acids are added in the N-to-C direction by linking the N-terminus of the incoming amino acid to the C-terminus of the growing protein chain. In vitro peptide synthesis, due to its complexity, proceeds in a precise, stepwise, and cyclic manner. Despite variations among commonly used peptide synthesis methods, they all share this sequential approach, adding amino acids one at a time to the peptide chain.

Included in your custom peptide synthesis order

Peptide synthesis method	Fmoc solid-phase synthesis (standard)GMP peptide synthesis (upon request)		
Quantity	From 1 mg to 1 kg		
Purity	Crude to ≥ 98%TFA removal upon request		
Lead time	Starting from 10 business days		
Shipping	Ambient temperature		
Peptide order	Lyophilized peptide and corresponding QC report		
Standard QC report	 Amino acid sequence Purity and quantity information Modification and conjugation information MS and HPLC profiles (except for crude/desalted peptides) 		
Additional analysis (upon request)	 Net peptide content analysis (N%) Qualitative amino acid analysis (AAA) Water content analysislon chromatography analysis (TFA, HAC) Solvent residue (DMF, ACN) Endotoxin (<1EU/MG) 		
Solubility test (upon request)	Request a solubility test to forgo the need to use part of your stock for testing. If you prefer to make it at your facilities, check our useful guidelines below.		

Quote request





PROTEIN PRODUCTION



We specialize in the production and purification of proteins using various expression systems. Our expertise covers multiple approaches, allowing us to adapt to different research and industrial needs. In this presentation, we will explore the following key areas:

- Production and purification of proteins in prokaryotic systems
- Production and purification of proteins in eukaryotic systems
- Cell-Free Protein Expression
- Expression of difficult proteins: challenges and solutions

Production and purification of proteins in prokaryotic systems

We specialize in producing recombinant proteins in E.Colis and B.subtilis tailored to your project needs.



Expression vector construction

- Gene synthesis including codon optimization for E. coli production.
- Gene subcloning in a high producing expression vector.



E. coli strain transformation

Transformation of the plasmid into various bacterial strains.





Test of 32 protein expression conditions

- Evaluation of 32 protein expression conditions (temperature, induction time, fractions).
- Determination of the best protein production conditions.
- Protein purification tests.





Protein expression scale up and purification

 1L protein expression and purification with optimized conditions previously determined.





QC analysis

- SDS/PAGE analysis and WB.
- Quantitative analysis by Bradford method.



Production and purification of proteins in eukaryotic systems

Use of an eukaryotic system allows to produce recombinant proteins that are submitted to post-traductional modifications, essentials to their functions. Indeed, all of these modifications belong to the normal maturation process that give a well-structured recombinant protein whom physical properties are different than just the gene-encoded protein.

These modifications, among others, are glycosylation, cleavage, methylation etc...

Our Production Organizations

We can produce these recombinant proteins in different eukaryotic systems such as: :

- Mammalian cells (CHO, HEK293, BHK)
- Yeast
- Insect cells (through Baculovirus transfer)

Quote request



Cell-Free Protein Expression

Cell-free protein synthesis (CFPS) is a method for protein expression that enables the production of target proteins without relying on living cells.

In this approach, a solution containing all the essential cellular components required for protein synthesis (e.g., ribosomes, tRNAs, enzymes, cofactors, amino acids, etc.) is used to transcribe and translate an input nucleic acid template, such as plasmid DNA, linear DNA, or mRNA. CFPS allows for the rapid generation of desired proteins within just a few hours, in contrast to traditional in vivo protein expression methods, which can take several days or longer.

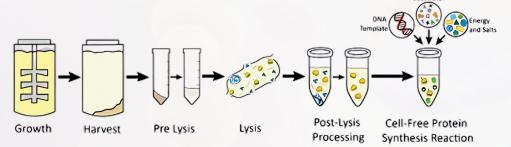


Figure: General workflow for preparation of cell-free extract and set up of CFPS reactions. A visualization from cell growth to the CFPS reaction is depicted above for a new user, highlighting the main steps involved.(1)

Cell-Free systems are advantageous for producing complex proteins.

Simplify your process with no need for cell cultivation, no more toxicity during cultivation! This open system allows addition of additives, thus creating an environment favorable to protein folding.

High-throughput productions available! Adapted for proteins like: Membrane proteins, cytotoxic proteins, complex folding proteins, viral proteins antigen for antibody generation and more broadly proteins which are difficult to express in classic systems.

Rapid Production: Get your proteins quickly with fast synthesis times (1 week for large-scale production)!

Efficiency: Directly use DNA templates for efficient protein production. A powerful technology to make proteins that were previously difficult to produce.

What are the advantages of cell-free protein synthesis (CFPS) systems compared to cell-based systems?

- CFPS is cost-efficient, as it eliminates the need for specialized facilities for bacterial or cell cultures. It is also fast, completing protein synthesis in just 3 hours, and offers easy control. Additionally, CFPS systems allow for real-time monitoring and modification of protein synthesis reactions.
- As an open system, CFPS enables precise control of reaction conditions and scalability of production. For example, adding metal ions (such as Fe²⁺, Mn²⁺, and Cu²⁺) can enhance the accurate synthesis of proteins. CFPS systems can also serve as a platform for producing toxins, such as antimicrobial peptides.
- The open nature of CFPS is particularly beneficial for prototyping new metabolic pathways and genetic circuits, providing controllable chemical enzymatic reactions among active substances.

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Expression of Difficult Proteins: Challenges and Solutions

Many proteins are difficult to express in heterologous systems due to factors like improper folding, codon usage differences, and lack of necessary post-translational modifications. Challenges include membrane protein integration, solubility issues, and toxicity. Solutions vary but often involve engineered host strains, optimized expression conditions, and specialized protein tags.

Key focus areas in difficult protein expression:

- Disulfide-bonded Protein Expression
- Membrane Protein Expression
- Toxic Protein Expression
- Target Protein Insolubility

Solutions: Approaches to Optimization

Developing a reliable procedure to express high-quality target proteins often requires systematic optimization. There is no universal "one-size-fits-all" solution, so the expression and purification process must be carefully tailored for each protein. Below, we illustrate the optimization of key components in the recombinant protein expression workflow.

Suitable Hosts

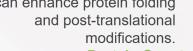






Vectors & Conditions

Selecting the right host cell can enhance protein folding modifications.





Using the right vectors and optimizing culture conditions can increase yield and stability.



removing destabilizing





Purification

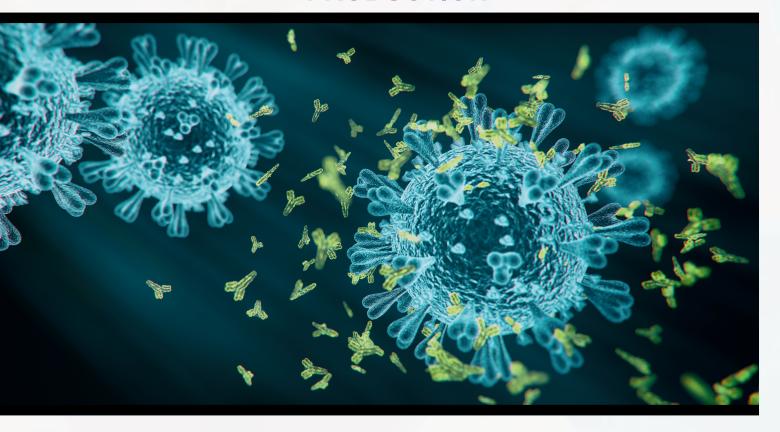
Adjusting purification parameters optimizes extraction and stability.

regions improves stability and expression.

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MONOCLONAL AND POLYCLONAL ANTIBODY PRODUCTION



Antibodies are indispensable tools in biomedical research, diagnostics, and therapeutic development. At Clinisciences, we provide state-of-the-art **monoclonal and polyclonal antibody production services**, ensuring high specificity, affinity, and reproducibility tailored to your research and clinical applications.

Our expertise extends to bispecific antibody production, allowing for the generation of next-generation therapeutics with enhanced targeting capabilities. Additionally, we offer antibody modification services, enabling functionalization, conjugation, and humanization for diverse applications. For structural and functional characterization, our antibody sequencing solutions provide precise insights into antibody composition, supporting discovery and development projects.

With cutting-edge technologies and a commitment to scientific excellence, we deliver high-quality antibody solutions designed to accelerate your research and biopharmaceutical advancements.

Monoclonal antibodies production



Llama monoclonals production

Our optimized library construction and screening processes with phage display technology guarantee successful isolation of high affinity VHH clones in a short time.

Advantages of Llama VHH Single Domain Antibodies

- Small size (15kD) allows access to hidden epitopes, including enzyme active sites.
- Enhanced tissue penetration, even crossing the blood-brain barrier.
- High stability under extreme conditions (heat, acidity) with the ability to refold after denaturation.
- Superior solubility due to increased hydrophilicity.
- Ideal for therapeutics and diagnostics due to their small size and robustness.

VHH Single Domain Antibody Production

- Llama Immunization: ELISA-monitored serum collection with preserved PBMCs for library construction.
- Phage Display & Screening: Affinity selection, ELISA validation, and sequencing of top clones.
- Large-Scale Purification: ~100μg of purified VHH per clone included; additional available.
- Naïve VHH Library: 2×10⁹ diverse clones from 20 non-immunized llamas.



Mouse or Rat monoclonals production

Hybridoma-based generation of high-affinity, highly specific monoclonal antibodies for research, diagnostics, and therapeutics.

Standard protocol:

- Immunization
- Fusion of B-cells with myeloma cells
- ELISA screening
- Sending of positive supernatants to the customer in order to make him testing the different clones in their own applications
- Cloning of hybridomas selected by limit dilutions
- Shipment of hybridomas and culture supernatants

Key numbers:

- Number of species : 5
- Number of shipped hybridomas: 2-5
- Number of shipped hybridomas supernatants : 2-5
- Delay of prestation : 4-5 months



Mouse monoclonals production after genetic immunization

This technique allows to make the mouse express in vivo the gene coding for the antigen of interest.

The gene-containing plasmid is injected into mice, leading to in vivo antigen expression. APCs present it via MHC, activating B-cells to produce specific antibodies.

Standard Protocol (100-140 days)

- 1. Construct CMV-driven DNA expression vector.
- 2. Transfect HEK293 cells & prepare antigen extract.
- 3. Inject plasmid DNA into mice (3-5 times).
- 4. Collect blood & test sera for antigen titer.
- 5. If needed, boost (1-2 times); proceed to hybridoma development if titer is sufficient.

Key Numbers

- Mice: ≥4
- Injections: 3-5
- Antigen per injection: 20 μg/mouse



Rabbit Monoclonal Antibody Production

Useful in a large number of techniques, they are clearly specific and affine to their target. Due to their high diversity, they can focus many new epitopes than current monoclonals. Different services are proposed:

Service 1: Isolation of B-cells

Standard protocol:

- Isolation of B-cells from rabbit spleens
- · Preparation of lymphocytes for fusion
- Option : Conservation of additional B-cells for 3 months in nitrogen

Service 2 : Development of rabbit monoclonal hybridomas

Standard protocol:

- · Fusion of B-cells with myelomas
- · ELISA screening against antigen
- Expansion of positive hybridomasand confirmation by ELISA
- Sending of positive supernatants to the customer for clone testing in their applications of interest.

Key numbers:

- Number of plates for screening: 40 (96 wells)
- Number of positive supernatants : 10-40
- Volume of positive supernatant sent to the customer: 1 mL

Service 3 : Sub-cloning of rabbit hybridomas

Standard protocol:

- Sub-cloning of hybridomas chosen by the customer
- Sending of sub-clones supernatants of each hybridoma to the customer
- Screening of the supernatants by the customer
- Expansion of chosen sub-cloned hybridomas and freezing of cells
- Sending of 1 part of the cells to the customer and stocking of the other part in the supplier.

Key numbers:

- Number of sub-cloned hybridomas: 1-3
- · Number of sub-clones by hybridomas: 10
- Volume of positive supernatants sent to the customer: 1 mL
- Number of tubes sent/stocked: 2/3

Monoclonal antibody library production

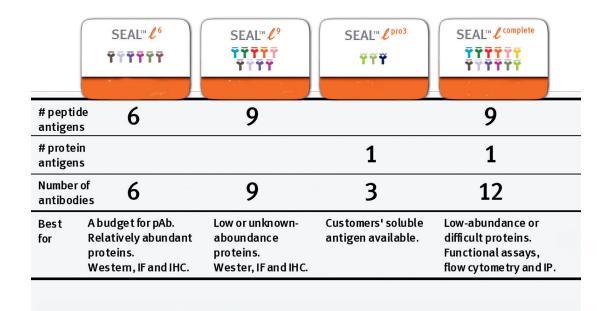
SEAL™ (Surface Epitope Antibody Library) technology enables the generation of high-affinity monoclonal antibodies targeting both linear peptides and conformational epitopes on protein surfaces. A typical SEAL™ library comprises 6-12 antibodies recognizing 4-8 distinct epitopes, significantly enhancing the likelihood of successful antibody discovery compared to traditional methods that focus on 1-3 epitopes. This approach has proven especially effective for challenging targets such as membrane receptors and transcription factors.

Advantages of SEAL™ Technology:

- Comprehensive Epitope Coverage: Targets a broad range of epitopes, increasing the chances of identifying functional antibodies.
- Enhanced Success Rates: Studies have shown that SEAL™ antibodies are 2-4 times more successful in applications like Western blotting, immunoprecipitation, and functional assays.
- Efficiency and Cost-Effectiveness: Offers significant time and cost savings over traditional monoclonal and polyclonal antibody generation methods.

SEAL™ Library Generation Process:

- Antigen Design: Utilizes proprietary computational models to identify exposed ten-residue sequences on the protein surface, achieving 73% accuracy in epitope prediction.
- Immunogen Preparation: Synthesizes genes encoding multiple SEAL™ epitopes, incorporating Immunogenicity Enhancement Factors (IEFs) to enhance immune response when expressed in E. coli.
- Immunization: Mice are immunized with the prepared immunogens, eliciting high-affinity IgG responses within three weeks.
- **Hybridoma Development**: Hybridomas secreting antibodies with nanomolar affinity are selected and cloned to establish stable cell lines.
- SEAL™ libraries are customizable, differing in the number and type of antigens used, the number of targeted epitopes, and the quantity of antibodies produced, ensuring alignment with specific research objectives.
- For more detailed information or to request a quote, please visit our Monoclonal Antibody Library Production page.





Polyclonal antibodies production

This prestation is realized from peptide, recombinant protein, cDNA (genetic immunization), small organisms, haptens, protein extracts etc...

Animal	Peptide Design	Peptide Synthesis or Recombinant Protein Production	KLH Labeling (or Other Carrier)	Collection of Pre-Immune Serum	Immunization	Delivery of Immune Serum	Affinity Purification Against the antigen or
Rabbit	<		~	✓	✓	✓	Protein A
Goat	<		✓	✓	✓	✓	Protein G
Sheep	✓	✓	✓	✓	✓	✓	Protein G
Chicken	✓	✓	✓	✓	✓	✓	IgY-specific
Guinea Pig	<		~	✓	✓	✓	Protein A
Hamster	✓	✓	✓	✓	✓	~	Protein G
Donkey	✓	✓	✓	✓	✓	~	Protein G
Rat	<	✓	✓	✓	✓	✓	Protein G
Mouse	✓	✓	✓	✓	✓	✓	Protein G
Mouse (Genetic Immuniz ation)	✓	✓	✓	✓	✓	✓	Protein G

Key numbers:

						_
Animal	Minimal Number of Animals	Protocol Length	Number of Injections per Animal	Quantity of Antigen per Injection	Number of Sample Collections per Animal	Final Amount of Antibodies per Animal
Rabbit	1	50-90 days	5	150-300 µg	3	60-75 mL
Goat	1	80 days	5	150 μg - 1 mg	2	250-300 mL
Sheep	1	80 days	5	150 μg - 1 mg	2	250-300 mL
Chicken	2	70 days	4	100-250 μg	0	15-20 mg
Guinea Pig	3	50-70 days	4	100-250 μg	1	Varies
Hamster	3	70 days	4	100-250 μg	1	0.5-1 mL
Donkey	1	80 days	6	150-300 µg	1	Varies
Rat	2	35-70 days	3	100-300 μg	1	3-8 mL
Mouse	5	35-70 days	3	20-50 μg	1	0.3-1 mL
Mouse (Genetic Immuniz ation)	4	100-140 days	3-5	20 μg	1-2	Varies



Bispecific Antibody Production

Bispecific antibodies (bsAbs) are engineered immunoglobulins with two antigen-binding sites targeting distinct epitopes. One site targets a specific cell surface antigen on a target cell, while the other binds to a "triggering" molecule on an effector cell, such as Fcy receptors or the CD3/T-cell receptor complex. This dual specificity enables bsAbs to redirect effector cells toward target cells, bypassing immune evasion. BsAbs can trigger various cytotoxic responses and leverage functions like ADCC, phagocytosis, and complement activation. Currently, two bsAbs are approved for therapeutic use, with more in clinical trials for cancer and other diseases.

Advantages and Limitations of Bispecific Antibodies







Advantages

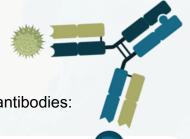
- Bispecific antibodies enhance cytotoxicity by directing effector cells to tumor cells.
- They can simultaneously recognize two molecular targets, improving selectivity, functional affinity, safety, and therapeutic efficacy.
- Development and clinical trial costs are reduced compared to combination therapy with two monoclonal antibodies.

Limitations

- Challenges in manufacturing due to potential mismatching between heavy and light chains.
- Non-natural structures may induce immunogenicity.

Production of Bispecific Antibodies

Numerous methods have been developed to generate bispecific antibodies:



Hybrid Hybridoma (Quadroma):

An early approach relying on the somatic fusion of two hybridoma cell lines producing murine IgGs with desired specificities. However, the yield of functional bispecific antibodies is unpredictable, requiring extensive purification.

Recombinant Techniques:

Bispecific IgG antibodies are formed from distinct heavy and light chains in the same system, requiring multiple plasmids. Separating HC and LC on different plasmids enables ratio optimization for efficiency. Stable clonal selection is labor-intensive but essential for large-scale production.

Transient Transfection:

Offers rapid results without genomic integration, facilitating early development. HEK293 and Expi293 cells are widely used for transient expression. Expertise in antibody engineering has enhanced production efficiency, ensuring high yields and functionality for therapeutics.

CliniSciences Production Scientists have the experience in producing a variety of IgG formats including Bispecific IgG.

Please contact us at tech@clinisciences.com for more information or for a quote request.



Antibody modification

we specialize in advanced antibody modification techniques to optimize functionality, specificity, and efficiency for research, diagnostics, and therapeutic applications. Our services include:

1. Antibody Conjugation

Enhance antibody functionality by attaching fluorophores, enzymes, biotin, or drug molecules for applications like flow cytometry, ELISA, and targeted drug delivery. We offer:

- ✓ Site-specific & random conjugation
- ✓ Enzymatic & chemical linking methods
- √ High-purity, ready-to-use conjugates

2. Antibody Fragmentation

Improve tissue penetration and reduce immunogenicity by generating Fab, F(ab')₂, or scFv fragments through enzymatic digestion or recombinant production. Ideal for:

- ✓ Immunohistochemistry & imaging
- √ Targeted therapeutics
- ✓ Biosensor applications

3. Antibody Engineering

Custom-engineered antibodies for higher affinity, stability, and functionality using cuttingedge techniques like humanization, Fc modification, and bispecific antibody design. Our solutions include:

- ✓ Affinity maturation
- ✓ Bispecific & multispecific antibody development
- ✓ Custom Fc engineering for enhanced effector functions

4. Antibody Purification

Achieve the highest purity and yield with our advanced antibody purification techniques, including:

- ✓ Protein A/G/L affinity chromatography
- √ Ion exchange & size exclusion chromatography
- ✓ Custom purification strategies for specific applications

We ensure high-quality, scalable solutions tailored to your needs. Please contact us at tech@clinisciences.com for more information or for a quote request.



Antibody Sequencing

We offer antibody de novo sequencing service. We directly sequence the antibody protein using multiple enzyme digestion and high resolution LC-MS/MS. Our service guarantees full length sequencing of the heavy and light chains.

Our sequencing process does not require hybridoma, mRNA, or other sequence information. It provides a direct and independent insight into your antibody sample.

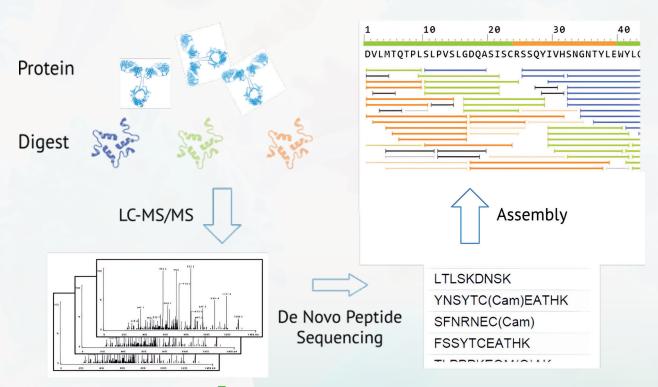
Accurate – We guarantee at least **5X coverage of CDRs in the variable regions**. Every amino acid in the CDRs is confidently supported by fragment ions in at least five MS2 scans. For isomeric Leu and IIe, we strive to make correct inference from enzyme specificity and statistics in antibody database.

Comprehensive – As an option, we offer comprehensive characterization of the antibody protein. Our service includes the analyses of PTMs, glycosylation, disulphide bridges, contaminants, and other aspects customized to your needs.

Efficient – We use minimal amount of antibody sample (0.2 mg) and deliver results within 15 business days with consistent quality.

Method

- Our standard procedure consists of the following steps.
- Digest the antibody protein into overlapping peptides with multiple enzymes.
- Analyze the digestions with LC-MS/MS using a Thermo Orbitrap mass spectrometer.
- Characterize overlapping peptides with de novo peptide sequencing.
- · Automated antibody sequence assembly from characterized peptides.
- Result examination and annotation by our scientists.



PROTEIN ANALYTICS



We offer a range of analytical methods utilizing multiple assay platforms that be used to characterize a broad range of proteins expressed and purified by various methods. Our team will work closely with you from concept through delivery. Together, we'll develop a set of project deliverables tailored to your specifications of scale, purity, activity and other analytical characteristics on a timeline that meets your needs.

SDS-PAGE · SEC-HPLC

Optical density

Protein analytics

Aggregation status

Protein mass (Agilent HPLC-CHIP/QTOF)

- · Accurate mass: proteins, proteindrug conjugates
- Peptide and Glycan mapping
- Determination of post-translations modifications either in known or unknown samples.
- Standard COAs

Protein stability

- Tm&Tagg
- ΔG
- Isothermal stability
- Thermal recovery
- Sizing&polydispersity
- · Sizing with thermal ramp
- B22&kD
- Viscosity

Protein integrity and structure

- SEC-HPLC
- SDS-PAGE
- N-glycan analysis
- Western Blot

Protein activity

- Binding affinity (FortéBio Octet® RED96 System)
- Enzyme activity
- · Cell-based assays
- In vivo testing

Please contact us at tech@clinisciences.com for more information or for a quote request.

Contatc us







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