Applied Protein Services
A Window into the Future

Development risk and attrition rates remain two of the greatest challenges to a successful biopharmaceutical pipeline. To help its customers mitigate both aspects, Lonza launched Applied Protein Services – a platform of immunogenicity, stability and protein engineering services that can provide a window into the future of a biologic.

Improve Your Biologic Development Success

The Applied Protein Services platform is effective at improving the quality, safety, efficacy and manufacturability of antibodies, therapeutic proteins, peptides and vaccines. By supporting the successful selection, optimization and early process development of promising drug candidates, Lonza’s Applied Protein Services improves your likelihood of biologic development success.

Customer Services Available

- Algonomics Epibase™ & Algonomics Epibase IV™
  - Computer-based and cellular immunoprofiling for lead selection, lead comparison, optimization and surveillance

- Tripole™ Protein Engineering
  - Technology platform for protein structure analysis, modeling, engineering, deimmunization and antibody optimization

- AggreSolve™
  - Technology platform to help resolve protein aggregation and stability challenges

For more information, please contact one of Lonza’s Applied Protein Services experts at AppliedProteinServices@lonza.com
Algonomics Epibase™

*In silico* Immunogenicity Assessment Platform

Algonomics Epibase™ is a patented, award-winning T-cell epitope screening platform that analyzes and predicts the potential immunogenicity of protein leads. It supports the design, selection, and optimization of protein therapeutics with minimum risks for immunogenicity at their earliest development stage.

**Applications**
- T-cell epitope identification
- Immunogenicity profiling and comparison of protein leads
- Selection of low immunogenic protein therapeutics
- Deimmunization: reduce immunogenicity of protein drugs by T-cell epitope elimination
- Documentation of expected immunogenicity for risk management planning
- Design of highly immunogenic vaccines

**Advantages of Algonomics Epibase™**

Algonomics Epibase™ uses a "structural bioinformatics" approach; it searches for potential epitopes in the target protein based on the structural characteristics of HLA receptors and their peptide-binding properties.

**Broad Population Coverage**

Algonomics Epibase™ addresses immunogenicity in a global context (>98% coverage), including the HLA allotypes representative for the genetic variation in Caucasian, Asian, Hispanic, African American, and several other population groups. New HLA allotypes can be included upon request.

**High Accuracy**

Algonomics Epibase™ is significantly more accurate than sequence alignment-based methodologies because more structural information is used to compute the binding affinity of epitopes.

**Fast Screening**

Multiple drug candidates can be profiled at a very early stage of the development process, as the primary sequence suffices to perform the analysis.

**Cost-Effective**

T-cell epitope profiling of protein drugs is less time- and resource-consuming than comparable services.
Algonomics Epibase IV™

*In vitro* Immunogenicity Assessment Tool & Cellular Assays

Algonomics Epibase IV™ evaluates immunogenicity potential of protein or antibody therapeutics by directly measuring T-cell responses in human population using PBMCs. It identifies T-cell epitopes on proteins and allows direct comparison of immunogenicity profiles of protein leads. Combined with the Algonomics Epibase™ *in silico* tool, Algonomics Epibase IV™ cellular assays facilitate the selection of your best leads and helps support their further engineering. Up-to-date, *in vitro* T-cell activation assays are the closest one can get to address immunogenicity in humans prior to the first clinical application.

**Advantages of Algonomics Epibase IV™**

- Multi-parameter measurement of T-cell activation by flow cytometry, ELISPOT and other read-out methods that allow a detailed characterization of T-cell subtypes
- Medium-to-high throughput process capable of running a large amount of samples
- Stringent quality control assures assay consistency and traceability of each sample
- Constant supply of blood samples from healthy donors

**Applications**

**Protein Therapeutics**

- T-cell epitope characterization
- Ranking of protein leads based on their immunogenicity potential
- Comparison of protein immunogenicity
  - Modifications (pegylation, glycosylation)
  - Formulations
- Complementary data to preclinical animal tests for risk management plans
- Biosimilars: immunogenicity comparability studies
- Immune monitoring of patients in clinical trials complementary to ADA assessment

**Vaccines**

- T-cell epitope characterization and selection for both T-helper cells and CTLs
- *In vitro* vaccine efficacy evaluation
  - Ranking of vaccine leads
  - Complementary data to preclinical animal tests
  - Evaluation of extrinsic factors on vaccine immunogenicity
    - Modifications
    - Formulations
    - Immune monitoring of patients in phase 1 clinical trials

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**Steps of the Assay**

01: Blood collection and HLA typing (50 donors)

02: PBMC Isolation
- CD14+ Monocyte purification
- QC on viability and polyclonal activation potential

03: Evaluate direct drug effects on PBMCs

04: Identification of optimal parameters for T-cell responses
- Time kinetics: naive or recall responses
- Functional assays

05: Assay characterization on extended donor population

Healthy PBMCs

Dissect possible noise derived from product formulations (Buffers, etc.)

Optimized kinetics on whole proteins or peptides

Optimized multi-parameter measurement
Tripole™ Protein Engineering Platform

Tripole™ is Lonza’s proprietary technology platform for protein structure analysis, modeling, engineering, deimmunization, and antibody optimization.

This unique tool is routinely used in two modes:
1. Tripole™ identifies desirable molecular substitutions that modify or enhance its properties such as its activity, affinity, specificity, stability or protease resistance. In conjunction with Algonomics Epibase™, it can remove immunogenic hotspots.
2. Tripole™ unravels how a protein or protein assembly is organized and interacts with receptors or ligands.

Our Structural Bioinformatics Advantage
— FASTER, a patented algorithm for accurate side-chain modeling
— Annotated structure database of over 1,000 antibody-antigen complexes

Applications
Protein & Antibody Structure Analysis
Empowered with state-of-the-art techniques in homology modeling (dead-end elimination, FASTER), Tripole™ enables Lonza scientists to:
— Search structural similarities between proteins and build accurate 3-D structures by homology
— Analytically compute surfaces and packing interactions
— Study the dynamics, flexibility and energetics of a protein/ligand system
— Dock a ligand onto a protein and rationalizes experimental data related to protein-ligand interaction

Antibody Engineering
In the hands of experienced scientists, Tripole™ excels in antibody structure analysis and modeling. It has been applied extensively to improve structure and biological activities of proteins and antibodies, thus creating new IP for customers.

— VH, VL Structure Modeling
— CDR Conformation Modeling
— Exploration of Best VH, VL and CDR Combinations
— Generating Feasible Antibody Structures
— Structure building
— Antibody maturation guided by in silico modeling
— Antibody humanization and deimmunization
— CDR grafting
— Surface veneering
— Deimmunization: Identification of substitutions that eliminate T-cell epitopes while preserving protein structural integrity

Protein Engineering
Different in silico tools are combined to optimize protein structure properties and create the best protein leads with a minimum risk of immunogenicity.
For further information on Applied Protein Services please contact:

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More details can be found at:
www.lonza.com

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