

**MASS  
SPECTROMETRY  
SERVICES  
MSP**  
Version 10NO11

# **MASS SPEC SERVICES**

**PROTEOME PHOSPHOSITE PROFILING  
CUSTOMER INFORMATION PACKAGE**

**For tracking global changes in  
protein phosphorylation in lysates  
from tissues and cells treated in vivo**

**Toll free: 1-866-KINEXUS or 604-323-2547**

**Facsimile: 604-323-2548**

**E-mail: [info@kinexus.ca](mailto:info@kinexus.ca)**

**[www.kinexus.ca](http://www.kinexus.ca)**

**KINEXUS**



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# KINEXUS PROTEOME PHOSPHO-SITE PROFILING BY MASS SPECTROMETRY SERVICE

## INTRODUCTION

Protein phosphorylation is the most ubiquitous and conserved form of post-translational modification in living cells ranging from bacteria to humans. Most mammalian proteins are subject to phosphorylation at multiple sites. Kinexus estimates that there may be around 700,000 phospho-sites in the human proteome, and we have annotated about 93,000 experimentally confirmed phospho-sites in over 14,000 human proteins in our PhosphoNET website ([www.phosphonet.ca](http://www.phosphonet.ca)). Because protein phosphorylation is reversible and transient in nature, it allows rapid control of diverse cellular activities in a highly integrated and coordinated fashion. Phosphorylation can affect protein function by altering its stability, affinity for other proteins, cellular location and catalytic activity. This in turn allows essential events such as cell growth, division and even death in accordance with environmental conditions. By the very nature of the rapid appearance and lability of phospho-sites, the study of phosphoproteomics is faced with difficult challenges in its analysis. The methodologies adopted by Kinexus addresses many of these issues, including the actions of protein kinases and phosphatases post-homogenization and the low stoichiometry of protein phosphorylation events.

### 1. GENERAL METHODOLOGY

Proteome-wide phospho-site profiling by mass spectrometry (MSPP) has been made feasible due to the convergence of two recent technological advances. The first is the improvement in sensitivity and resolution of modern mass spectrometers, allowing accurate mass measurements of peptides in femtomolar to attomolar concentrations at resolutions better than 0.1 Da in 1000 Da. The second, is the advent of high throughput DNA sequencing leading to whole genome sequence data for a wide range of species including mouse, rat, and human. By obtaining accurate masses of peptides and matching these to predicted gene product masses, the identity of an unknown protein can often be determined.

The overall approach Kinexus has taken to large-scale protein phospho-site profiling studies is outlined in Figure 1, adapted from Rogers *et al.* (2010)<sup>1</sup>. To address the low stoichiometry of protein phosphorylation events, a technique called stable isotopic labeling with amino acids in cell culture (SILAC) is employed to greatly improve the ability of the MS methods to detect changes in phosphorylation states. The SILAC technique essentially allows semi-quantitative comparisons of phosphopeptides. Cells in the untreated control arm of the experiment are grown in normal isotope amino acids, and the treated arm is labeled during cell culture with the “heavy” isotopes <sup>2</sup>H, <sup>13</sup>C, and <sup>15</sup>N. This allows the relative differences between light and heavy phosphopeptides to be compared in the final MS stage. Phosphatases released from upon cell lysis can quickly and substantially reduce the signal from a given stimulus. The most common means of inhibiting phosphatases is through the use of commercially available inhibitors, but studies have shown that these inhibitors are marginally effective. Recent results using a combination of heat denaturation and chaotropic agents have shown to be much more effective. Prefractionation of the pooled labeled trypsin digested peptides allows adequate resolution of the large number of phosphopeptides in one MS run. This prefractionation is achieved by isoelectric focusing (IEF) due to its high loading cap and high

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<sup>1</sup> Rogers et al. 2010. An integrated global strategy for cell lysis, fractionation, enrichment and mass spectrometric analysis of phosphorylated peptides. *Mol. BioSyst*, 6: 822–829  
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Customer Information Package

recovery rate. Enrichment for phosphopeptides over nonphosphopeptides is done using a metal oxide chromatography step with  $\text{TiO}_2$ . Finally, phosphopeptide measurement by LC-MS/MS is carried out with optimized liquid chromatography gradients and MS/MS fragmentation schemes to minimize the neutral loss of phosphate from the phosphopeptides during mass spectrometry.

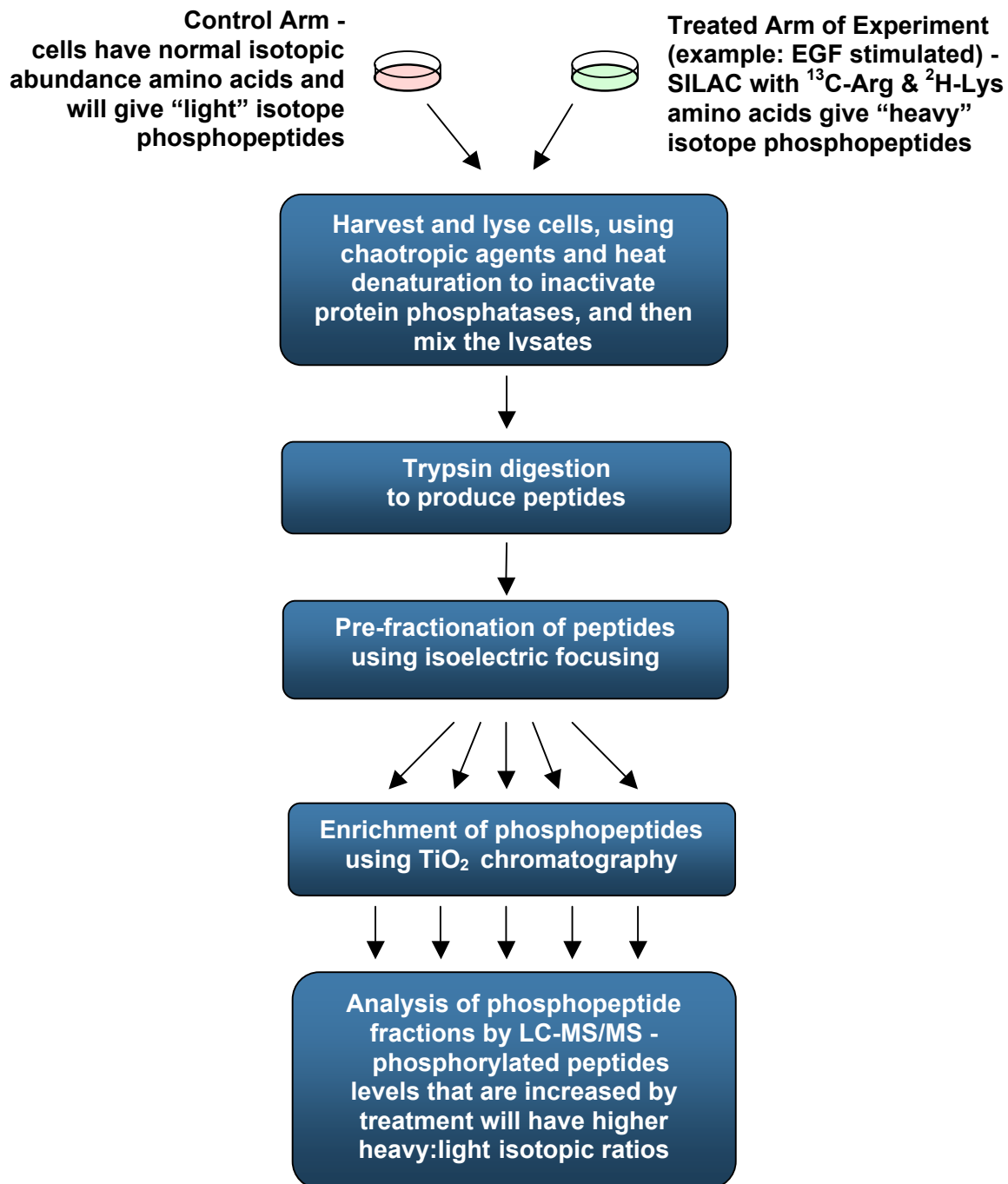


Figure 1. Methodology for proteome-wide phospho-site profiling studies.

## 2. EXAMPLE OF A PHOSPHOPROTEIN PROFILING STUDY – Effects of EGF Stimulation on Phosphoproteins in HeLa cells

Figure 1 outlines the steps in a basic proteome-wide phospho-site profiling study consisting of HeLa cells stimulated by epidermal growth factor (EGF). The methodology is adapted from Rogers et al 2010 <sup>1</sup>.

The control sample of the experiment consisted of untreated HeLa cells grown in media with normal isotopes of H, C, or N. The treated arm underwent stable isotope labeling with amino acids in cell culture (SILAC) and consisted of EGF-stimulated HeLa cells grown in media with <sup>2</sup>H, <sup>13</sup>C, or <sup>15</sup>N “heavy” isotopes of arginine and lysine. Typically for phosphopeptide mass spectrometry, each sample analysis needs about 15 mg of total cell lysate, so for HeLa cells, this required about 3 to 5 culture plates 150 mm in diameter. For the treated sample, the HeLa cells were harvested after 10 min of EGF stimulation. Cell harvesting was carried out by washing, scraping, and collecting the cells by centrifugation at low speed. Then the cells were resuspended in a lysis buffer containing the chaotropic agent sodium deoxycholate and subsequently heated to 99°C for 5 min. Protein samples in solution were then digested with trypsin and desalted. The resulting peptide solutions were initially separated by in-solution isoelectric focusing (IEF) along a pH gradient from 3 to 10 and collected in 10 fractions. This fractionation and concentration of the sample peptides before mass spectrometry allows a much deeper analysis of components of the proteome. To enrich for phosphopeptides, which are predominantly negatively charged, each IEF fraction was acidified and loaded onto a TiO<sub>2</sub> micro-column, washed, and then eluted with 0.5% NH<sub>4</sub>OH and acetonitrile. The phosphopeptide enriched eluates were analyzed by LC-MS/MS on an Agilent 1100 nanoflow HPLC coupled online to a LTQ-OrbitrapXL (Thermo Fisher Scientific). A simpler collision induced dissociation MS<sup>2</sup> scheme was used over the more complicated MS<sup>3</sup> and multistage activation schemes. Peak mass-to-charge lists were searched against a database containing all human protein sequences in the International Proteome Index using Mascot (v2.2, Matrix Science).

This type of study was able to identify approximately 6000 phosphorylation sites and characterize their response to EGF treatment of the HeLa cells.

Further information and instruction is provided with this MSPP Services Customer Information Package. Your careful review of this package will ensure that we can offer the highest level of quality in providing our unique proteomics services to you. We have requested a lot of information from you regarding the preparation of your cell lysate samples so that they are produced according to your specification and in the event that you choose our Non-Confidential Pricing option that we may share some of the data with other scientists in the future in PhosphoNET. For these rights, we have discounted our standard charges by ~33%. You should find that the proper entry of information into the various forms provided by Kinexus also useful for your own reference at a later date when you receive your MSPP results. Should you have any questions or concerns, we would be pleased to hear from you. Thank you in advance for letting Kinexus become one of your trusted research partners.

## SAMPLE PREPARATION

### 3. CELL AND TISSUE CULTURE

Culturing of cells for a large scale proteomics study using the methodology adopted by Kinexus requires stable isotope labeling with amino acids in cell culture (SILAC). It is recommended that this be carried out at the Kinexus facilities, so Kinexus will require a complete description of the experimental system when filling out the service identification form MSPP-SIF. The cell line and other specialized cell culture materials should be sent to Kinexus by FedEx courier (using the commercial invoice form in the appendix if shipping originates outside of Canada). Should the client prefer to carry out the cell culture, labeling, and harvesting themselves, then contact Kinexus technical support for more detailed instructions.

## SHIPPING AND PRICING

### 4. SHIPPING INFORMATION

**If shipping frozen cell line cultures the samples *must* be shipped on dry ice.** Approximately 5% of the time, it has been necessary for clients to re-send samples to Kinexus due to thawed samples at the time of arrival. This is most often due to insufficient dry ice for shipping and/or inadequate completion of shipping information.

The aforementioned procedure has been designed to reduce the use of shipping materials and courier costs, and to ensure that your precious samples arrive in a safe and stable form at our laboratory facilities. Note that clients are responsible for payment of courier costs. The sample vials should be sent to the address listed below by any express courier that accepts dry ice shipments. We recommend Federal Express for shipments originating in North America, and World Express is the preferred courier choice outside of North America. Ship the samples to the following address:

Kinexus Bioinformatics Corporation  
Suite 1, 8755 Ash Street  
Vancouver, B.C. Canada V6P 6T3

Telephone: (604) 323-2547  
Facsimile: (604) 323-2548  
E-mail [info@kinexus.ca](mailto:info@kinexus.ca)

Please ensure 3 copies of a signed commercial invoice accompany your shipment which specifies your samples are non-hazardous and non-infectious. Since the samples are not for resale, the value of your shipment should be priced at approximately \$1.00 per sample in order to avoid paying additional duties and taxes on entry into Canada. It is highly recommended that customers e-mail their courier airway bill number and the date of departure to [info@kinexus.ca](mailto:info@kinexus.ca) so we can track your shipment in transit and ensure it arrives in a timely manner. For shipping from outside of North America, we highly recommend send out on a Monday or Tuesday. We will send a confirmatory e-mail once your shipment arrives at our facility.



## 5. PRICING INFORMATION

Pricing estimates for typical phosphoproteomics studies are given in the service order form MSPP-SOF. A base phosphoprotein profiling study consists of one control arm and one treatment arm, each carried out in a single run. Pricing for additional replicates and treatment arms is also outlined in the MSPP-SOF.

Kinexus offers its services at different pricing levels depending on the level of confidentiality required for your samples. To receive a 33% discount, Kinexus requires the Client-Supplied Non-Confidential Sample Description Form (NSDF-LY) to be completed in full (Sections A-K) including species, cell line name, cell state, and treatment for each sample being analyzed.

For volume discounts or quotations for large orders, please contact the Director of Sales & Marketing at 1-866-KINEXUS (or 1-604-323-2547 (Extension 11 or Option 2 on the telephone directory) or e-mail [sales@kinexus.ca](mailto:sales@kinexus.ca).

## FOLLOW UP SERVICES AND FORMS

### 6. FOLLOW UP SERVICES

The identity of several thousand phosphopeptides and their associated proteins can present a herculean task for data interpretation. The Kinexus PhosphoNet KnowledgeBase (<http://www.phosphonet.ca/>) is a valuable free online resource for the initial interpretation of these phospho-sites and possible upstream kinases that catalyze their phosphorylation. Additional, more advanced data mining of the phosphoprotein dataset is available, such as prediction of possible protein-protein interactions for selected phosphoproteins and kinases that target novel phospho-sites not found in PhosphoNET. Please contact the Kinexus technical support personnel for further recommendations on data interpretation.

After phospho-sites have been identified with our MSPP services and putative kinases that target these sites identified through our bioinformatics services, clients may desire to have these predictions tested *in vitro*. Kinexus can produce recombinant forms of human target proteins or synthesize short peptides that are predicted from the amino acid sequence surrounding target phospho-sites. We use these proteins and peptides as substrates for testing with our panel of more than 360 human protein kinases. If desired, Kinexus can also help produce specific antibodies against desired phospho-sites. Contact our Customer Services Representative to learn more about these custom proteomics services or visit our website at [www.kinexus.ca](http://www.kinexus.ca).

## 7. INSTRUCTIONS FOR FORMS

All the necessary forms for the Mass Spectrometry Proteome Phospho-site Profiling (MSPP) services are provided in the Appendices section at the end of this Customer Information Package. Electronic fillable MS-Word versions of these forms are available by e-mail or phone request and may be directly downloadable from the Kinexus website. Please contact our Technical Service Representatives by e-mail at [info@kinexus.ca](mailto:info@kinexus.ca) or by phone at 604-323-2547 Ext. 1 for all enquiries related to technical/research issues, work orders, service fees or request of fillable order forms.

**List of Forms to be Completed - All customers are required to complete the following forms for each order placed:**

- A. Kinexus Proteomics Services Agreement - Customers are required to complete and sign our standard Proteomics Services Agreement before their first order can be processed. Unless otherwise specified, this Agreement is valid for all future orders with a standard term of 15 years.
- B. Service Order Form (MSPP-SOF). The Service Order Form allows us to track all of the various services to be used within an order.
- C. Service Identification Form (MSPP-SIF). The Service Identification Form permits us to determine which proteomics service screen is to be used for the analysis of two cell lysate samples together.
- D. Sample Description Forms (NSDF-Cell, NSDF-C, CSDF-C). These forms provide descriptions of the cell lines and treatment agents to be used for the MSPP Service if these are provided by the client.
- E. Commercial Invoice (if client is sending samples to Kinexus from outside of Canada).
- F. FedEx Air waybill obtained from FedEx (if client is sending samples to Kinexus by courier).

All orders should have as a minimum: of one SOF and one SIF form completed, along with a courier airway bill if the customer is sending cell culture and treatment compound materials and a commercial invoice if the customer is sending materials from outside of Canada. A new Kinexus Service Agreement is not necessary if the client has previously placed an order with Kinexus and submitted a signed Kinexus Service Agreement at that time.

### Instructions for Specific Forms

#### A. Kinexus Proteomics Services Agreement

- A Kinexus Service Agreement is required to be signed before the first order can be processed
- This Agreement is required to be signed and dated by an authorized representative, typically a Senior Officer, Senior Scientist, or Principal Investigator, before the first order can be processed, but does not have to be signed again for repeat orders. The Kinexus Service Agreement is typically valid for 15 years. If you require changes or modifications to be made to our standard Service Agreement, please email us at [sales@kinexus.ca](mailto:sales@kinexus.ca) to request a Microsoft Word version of the document so your requested changes can be made directly into the agreement and emailed to us for our final approval



## **B. Service Order Form (MSPP-SOF)**

- Please ensure that shipping address and contact name and numbers are specified
- Pricing information is for estimation purposes. Final pricing will require review of the study by Kinexus. Any promotional vouchers or quotations should be listed in this pricing section
- Include a Purchase Order, Visa or MasterCard number for payment
- The form is signed and dated

## **C. Service Identification Form (MSPP-SIF)**

For each sample submitted, please ensure the following:

- In Section A, the customer must assign a unique Client Study Identification Name that provides a connotative label for the customer
- In Section B, describe the experimental system to be used for this phosphoproteomics study
- For Section C, estimate of pricing is given in the MSPP-SOF
- The form is certified correct and signed and dated

## **D. Sample Description Forms (NSDF-Cell, NSDF-C, CSDF-C) (if client is providing a cell line or compounds for treatment)**

### ***Client Supplied Cell Line Description Form (NSDF-Cell)***

- The cell line that you are submitting for propagation and treatment at Kinexus must be identified along with special instruction on how the cells are to be cultivated and treated.
- Please identify any safety concerns related to the cell line and treatment
- The form is certified correct and signed and dated

### ***Client Supplied Non-confidential Sample Description Form for Compounds (NSDF-C)***

### ***Client Supplied Confidential Sample Description Form for Compounds (CSDF-C)***

For any compound or protein samples submitted, please ensure the following:

- In Section A, the customer must enter the unique Client Screen Identification Name from Box A of the Mass Spectrometry Proteome Phospho-site Profiling Service Identification Form (MSPP-SIF) to match the sample agent to the particular analysis performed with this sample.
- Your sample agent (compound or protein) used for treatment of cells is described by completion of Client Supplied Non-Confidential (NSDF-C) or Confidential (CSDF-C) Sample Description Forms by checking the appropriate boxes and entering the appropriate information requested in Sections A-K for Non-confidential samples and Sections A-C for Confidential samples
- The form is certified correct and signed and dated

- Note that the information provided on the NSDF-C form may be shared with thousands of other scientists in the future with the Non-confidentiality pricing. In the spirit of collegiality, please be as accurate as possible in completing the NSDF-C form in order not to handicap their research efforts should they desire to follow up on your mass spectrometry results.

#### **E. Commercial Invoice (not required by Canadian customers)**

*Please complete the attached commercial invoice with the following information:*

- Date of exportation
- Shipper/Exporter name, address, phone number
- Country of export/Country of origin
- Name of courier and the airway bill number
- Number, type and total weight of package(s)
- Total declared value of shipment (number of samples x \$1.00 per sample) and please specify currency
- Date, name, signature, and title of authorized person

*Include three (3) copies of the commercial invoice with the airway bill*

**NOTE: Do not change the value of your shipment to more than \$1.00 per sample as this will prompt the custom brokers to charge Kinexus with a duty and GST fee on your package. Since the samples are processed internally and not returned to the customer or resold, there is no real commercial value.**

The international air waybill is required for all international shipments between Canada and the rest of the world. It is also your Customs Declaration, which can possibly be used to clear your shipment through customs at the destination. The customs clearance process begins with the description of the air waybill. If the description is too vague or missing, customs authorities may select the shipment for further inspection. All customs paperwork, such as the commercial invoice, must have detailed commodity descriptions. A detailed description on the air waybill and other customs documentation will help speed up the clearance time and reduce your delivery time. In the event that Kinexus must go to a Canada Customs facility to claim the package of samples for client order due to inadequate completion of the commercial invoice, additional charges will apply.

#### **F. Airway Bill for Federal Express or any courier that accepts dry ice shipments (not supplied with this package)**

*Complete an airway bill and specify:*

- Priority overnight delivery
- Bill transportation charges to your institute
- Place sufficient dry ice to last several days into a Styrofoam shipping container
- Seal the edges of the Styrofoam container with tape to preserve dry ice longer

- Dry ice is a “*hazardous*” item, so ensure proper labels are attached to the outside of the box;
- **Do not specify Saturday delivery or hold at courier location**
- For Federal Express shipments telephone 1-800-GO-FEDEX or visit them on-line at [www.fedex.com](http://www.fedex.com) or [www.fedex.ca](http://www.fedex.ca) to schedule a pick up or complete your forms
- For shipments coming from within Canada or the United States, please ship any day from Monday to Wednesday. **Do not ship on a Thursday or Friday.**
- For international shipments coming from outside of North America, the best day to ship is on a Monday to ensure arrival in Canada for delivery later the same week
- It is recommended that customers e-mail the date of your shipment and the courier airway bill number with number of samples to Kinexus at [info@kinexus.ca](mailto:info@kinexus.ca) to ensure we can track your package should it get held up in Canadian Customs
- For any customer located outside of Canada, 3 copies of a commercial invoice is required to accompany your shipment (see below)



KINEXUS

Form: MSPP-SOF

MASS SPECTROMETRY
PROTEOME P-SITE PROFILING

SERVICE ORDER FORM

Subject to terms of the Kinexus
Proteomics Services Agreement

KINEXUS ORDER NUMBER
For Kinexus internal use only.

CUSTOMER INFORMATION [ ] REPEAT CUSTOMER OR [ ] NEW CUSTOMER

Form fields for customer information including Name of Authorized Representative, Title/Position, Company Name, Department, Street Address, City, State or Province, Country, Zip or Postal Code, Email Address, Telephone Number, and Contact Person.

STUDY REPORTS

RESULTS SENT BY EMAIL TO: [ ] AUTHORIZED REPRESENTATIVE/INVESTIGATOR AND/OR [ ] CONTACT PERSON

PRICING INFORMATION

The Mass Spectroscopy Proteome Phospho-site Profiling services utilize large-scale, semi-quantitative techniques that enrich for and identify phosphorylated peptides...

Pricing table with columns for service description, unit price, and total cost. Includes subtotal and estimated total cost for this order. Also includes a section for Canadian customers with HST information.

PAYMENT METHOD

[ ] PURCHASE ORDER ACCEPTED FROM COMPANIES AND INSTITUTES WITH APPROVED CREDIT. P.O. NUMBER:
[ ] VISA OR [ ] MASTERCARD

Fields for Print Cardholder Name, Visa Number, Expires (M/Y), and Cardholder Signature.

BILLING INFORMATION

[ ] SEND INVOICE TO CUSTOMER AT ABOVE ADDRESS OR [ ] SEND INVOICE TO ACCOUNTS PAYABLE CONTACT:

Form fields for billing information including Accounts Payable Contact Name, Company Name or Institute, Street Address, City, State or Province, Country, Zip or Postal Code, and Telephone Number.

AUTHORIZATION

CUSTOMER HAS READ THE KINEXUS PROTEOMICS SERVICES AGREEMENT AND AGREES TO BE BOUND BY THE TERMS AND CONDITIONS:

Fields for Print Name of Authorized Representative or Principal Investigator, Authorized Signature, and Date y/m/d.

How did you originally hear about the MSPP Services? [ ] Direct Mail [ ] Email [ ] Web Site [ ] Advertisement [ ] Referral [ ] Conference or Trade Show [ ] Other



# KINEXUS

Form: **MSPP-SIF**

## MASS SPECTROMETRY PROTEOME PHOSPHO-SITE PROFILING SERVICE IDENTIFICATION FORM

*Subject to terms of the Kinexus Proteomics Services Agreement*

**KINEXUS ORDER NUMBER**

**NAME:** \_\_\_\_\_  
*(Authorized Representative or Principal Investigator)*

**COMPANY/INSTITUTE:** \_\_\_\_\_

### MASS SPECTROMETRY PHOSPHOPROTEIN PROFILING SERVICE REQUESTED:

Presently, the Proteome Phospho-site Profiling methodology used by Kinexus requires a cell culture system due to the use of stable isotopic labeling with amino acids in cell culture (SILAC) to achieve sensitive semi-quantitative comparisons between phosphorylation levels in control versus treated cells. With the use of SILAC, it is necessary to culture cells in Arg-free and Lys-free media to ensure adequate labeling of cellular proteins with added "heavy" isotope Arg and Lys amino acids.

If your experimental cell system cannot be cultured in serum-free media, then Kinexus may not be able to conduct a phosphoproteomics study using present methods.

If you need assistance completing this form, please contact a technical service representative by calling toll free in North America 1-866-KINEXUS (866-546-3987) or by email at [info@kinexus.ca](mailto:info@kinexus.ca). An electronic fillable MS-Word version of this form can be downloaded from the Kinexus website at [www.kinexus.ca](http://www.kinexus.ca) or supplied upon request.

<input type="checkbox"/> <b>CUSTOM SERVICE REQUESTED:</b> The Kinexus Mass Spectrometry Phosphoprotein Profiling base study design consists of one control and one treatment carried out in singlet. It is expected, but not guaranteed, to identify several thousand phosphopeptides. Additional or supplemental studies consist of replicates of the base study or one additional treatment arm, or a combination of addition replicates or treatment arms.	<b>KINEXUS ID NUMBER</b> <i>(Bar Code Identification Number)</i> For Kinexus Internal Use Only.	<b>A. CLIENT <span style="background-color: yellow;">STUDY ID</span> NAME:</b> Customer ID: <i>Provide ID name of your choice for your reference.</i>
<b>B. EXPERIMENTAL CELL SYSTEM:</b> <i>Please attach a completed NCSD-cell form with a description of the experimental cell system to be used in the phosphoproteomics study, with attention to the following items.</i> <ol style="list-style-type: none"> <li>Cell species and cell line type, including special identification such as ATCC accession numbers or in-house cell line identifiers.</li> <li>Growth media and tolerance of cell line to serum free media.</li> <li>Typical cell line growth characteristics such as growth rate, passage frequency and method (trypsin-EDTA or scraping), cell density, and cell harvesting method.</li> <li>Stimulative or inhibitory treatment(s), describing the supplier and catalog number of the treatment compound or any specific equipment required for treatment, treatment concentration or intensity, and treatment duration, and cell stage at time of treatment.</li> <li>Additional special instructions or comments regarding cell culture or treatment.</li> </ol>	<b>C. PRICING:</b> <i>Please refer to pricing section of MSPP-SOF. Note that this is a preliminary estimate of the MSPP services costs.</i>	

\_\_\_\_\_  
Name of person completing this form

\_\_\_\_\_  
Signature

\_\_\_\_\_  
Date (Y/M/D)



KINEXUS

Form: NSDF-Cell

FOR CELL LINES

CLIENT SUPPLIED
NON-CONFIDENTIAL SAMPLE DESCRIPTION FORM

Subject to terms of the Kinexus Service Agreement

KINEXUS ORDER NUMBER

NAME: \_\_\_\_\_ COMPANY/INSTITUTE: \_\_\_\_\_
(Authorized Representative or Principal Investigator)

Cell Line Details:

Please refer to the Customer Information Package for the particular Kinexus proteomics service that you are requesting for details on how to prepare and ship your cells to Kinexus for cultivation and treatment. Clients are required to complete all Sections A-K if they provide their own cell lines for culture and analysis. If you need further assistance, please contact a technical service representative by calling toll free in North America 1-866-KINEXUS (866-546-3987) or by email at info@kinexus.ca. Please check the appropriate tick boxes.

Form sections A through K: A. CLIENT SCREEN ID NAME + KINEXUS SERVICES NAME; B. CELL LINE IDENTIFICATION; C. SPECIES ORIGIN; D. CELL SOURCE; E. TISSUE ORIGIN; F. ESTABLISHED CELL LINE; G. CELL SAFETY CONCERNS; H. DESIRED CELL STATE PRIOR TO TREATMENT; I. CULTURE MEDIA; J. TREATMENTS; K. ADDITIONAL CELL CULTURE AND TREATMENT INFORMATION.

I hereby certify that all the sample information provided in this order is correct and accurate to the best of my knowledge. I further acknowledge that I may be contacted by a Kinexus representative for additional information if any section is unclear.

Name of person completing this form

Signature

Date (y/m/d)



KINEXUS

Form: NSDF-C

CLIENT-SUPPLIED FOR COMPOUNDS NON-CONFIDENTIAL SAMPLE DESCRIPTION FORM Subject to terms of the Kinexus Proteomics Services Agreement

KINEXUS ORDER NUMBER

NAME: COMPANY/INSTITUTE: (Authorized Representative or Principal Investigator)

Non-Confidential Service Requested and Compound Sample Details:

Please refer to the Customer Information Package for the particular Kinexus proteomics service that you are requesting for details on how to prepare and ship your compounds to Kinexus for testing. Clients are required to complete Sections A and B and properly identify the compounds for examination for a non-confidential analysis with our proteomics services. For confidential analysis, clients should complete instead the Client-Supplied Confidential Sample Description Form NSDF-C. Use additional copies of this form if you have more than two compounds for testing. For each compound to be tested, please send enough material to complete the analysis. If you need assistance completing this form, contact a technical service representative by calling toll free in North America 1-866-KINEXUS (866-546-3987) or by email at info@kinexus.ca.

A. CLIENT SCREEN ID NAME + KINEXUS SERVICES NAME: CLIENT ID: KINEXUS PROTEOMICS SERVICES NAME: Use the Client ID Name that you entered in Box A on the Service Identification Form (SIF). Provide a distinct Client ID Name for reference for each different compound to be tested. The Kinexus Proteomics Services abbreviated name should be used from the SIF. KINEXUS ID NUMBER (FOR INTERNAL USE ONLY) (Bar Code Identification Number)

B. COMPOUND DETAILS: Compound name (required): Supplied form of compound Solid Liquid FOR SOLIDS PROVIDE: Mass (mg): Formula Weight: Is the compound or solution toxic? Yes No FOR LIQUIDS PROVIDE: Molarity: or Concentration: Volume: MSDS or safety sheets provided Yes No For solids, what is the recommended solvent? Is the compound soluble in water or 2% DMSO? Provide safety instructions and storage details for handling, or any other special information:

A. CLIENT SCREEN ID NAME + KINEXUS SERVICES NAME: CLIENT ID: KINEXUS PROTEOMICS SERVICES NAME: Use the Client ID Name that you entered in Box A on the Service Identification Form (SIF). Provide a distinct Client ID Name for reference for each different compound to be tested. The Kinexus Proteomics Services abbreviated name should be used from the SIF. KINEXUS ID NUMBER (FOR INTERNAL USE ONLY) (Bar Code Identification Number)

B. COMPOUND DETAILS: Compound name (required): Supplied form of compound Solid Liquid FOR SOLIDS PROVIDE: Mass (mg): Formula Weight: Is the compound or solution toxic? Yes No FOR LIQUIDS PROVIDE: Molarity: or Concentration: Volume: MSDS or safety sheets provided Yes No For solids, what is the recommended solvent? Is the compound soluble in water or 2% DMSO? Provide safety instructions and storage details for handling, or any other special information such as sensitivity to light, heat, freezing, and dilution.

I hereby certify that all the sample information provided in this order is correct and accurate to the best of my knowledge. I further acknowledge that I may be contacted by a Kinexus representative for additional details if the information provided is unclear.

Name of person completing this form Signature Date (y/m/d)





KINEXUS

Form: CSDF-C

FOR COMPOUNDS

CLIENT-SUPPLIED CONFIDENTIAL SAMPLE DESCRIPTION FORM

Subject to terms of the Kinexus Proteomics Services Agreement

KINEXUS ORDER NUMBER

NAME: \_\_\_\_\_ COMPANY/INSTITUTE: \_\_\_\_\_ (Authorized Representative or Principal Investigator)

Confidential Service Requested and Compound Sample Details:

Please refer to the Customer Information Package for the particular Kinexus proteomics service that you are requesting for details on how to prepare and ship your compounds to Kinexus for testing. Clients are required to complete Sections A and B, but do not have to identify the actual compound by name for examination for a confidential analysis with our proteomics services; however, a client-supplied coded name must be provided. Use additional copies of this form if you have more than two compounds for testing. For each compound to be tested, please send enough material to complete the analysis. If you need assistance completing this form, contact a technical service representative by calling toll free in North America 1-866-KINEXUS (866-546-3987) or by email at info@kinexus.ca.

A. CLIENT SCREEN ID NAME + KINEXUS SERVICES NAME: CLIENT ID: \_\_\_\_\_ KINEXUS PROTEOMICS SERVICES NAME: \_\_\_\_\_ Use the Client ID Name that you entered in Box A on the Service Identification Form (SIF). Provide a distinct Client ID Name for reference for each different compound to be tested. The Kinexus Proteomics Services abbreviated name should be used from the SIF. KINEXUS ID NUMBER (FOR INTERNAL USE ONLY) (Bar Code Identification Number)

B. COMPOUND DETAILS: Compound Name: \_\_\_\_\_ Supplied form of compound [ ] Solid [ ] Liquid FOR SOLIDS PROVIDE: Mass (mg): \_\_\_\_\_ Formula Weight: \_\_\_\_\_ Is the compound or solution toxic? [ ] Yes [ ] No FOR LIQUIDS PROVIDE: Molarity: \_\_\_\_\_ or Concentration: \_\_\_\_\_ Volume: \_\_\_\_\_ MSDS or safety sheets provided [ ] Yes [ ] No For solids, what is the recommended solvent? \_\_\_\_\_ Is the compound soluble in water or 2% DMSO? \_\_\_\_\_ Provide safety instructions and storage details for handling, or any other special information: \_\_\_\_\_

A. CLIENT SCREEN ID NAME + KINEXUS SERVICES NAME: CLIENT ID: \_\_\_\_\_ KINEXUS PROTEOMICS SERVICES NAME: \_\_\_\_\_ Use the Client ID Name that you entered in Box A on the Service Identification Form (SIF). Provide a distinct Client ID Name for reference for each different compound to be tested. The Kinexus Proteomics Services abbreviated name should be used from the SIF. KINEXUS ID NUMBER (FOR INTERNAL USE ONLY) (Bar Code Identification Number)

B. COMPOUND DETAILS: Compound Name: \_\_\_\_\_ Supplied form of compound [ ] Solid [ ] Liquid FOR SOLIDS PROVIDE: Mass (mg): \_\_\_\_\_ Formula Weight: \_\_\_\_\_ Is the compound or solution toxic? [ ] Yes [ ] No FOR LIQUIDS PROVIDE: Molarity: \_\_\_\_\_ or Concentration: \_\_\_\_\_ Volume: \_\_\_\_\_ MSDS or safety sheets provided [ ] Yes [ ] No For solids, what is the recommended solvent? \_\_\_\_\_ Is the compound soluble in water or 2% DMSO? \_\_\_\_\_ Provide safety instructions and storage details for handling, or any other special information such as sensitivity to light, heat, freezing, and dilution. \_\_\_\_\_

I hereby certify that all the sample information provided in this order is correct and accurate to the best of my knowledge. I further acknowledge that I may be contacted by a Kinexus representative for additional details if the information provided is unclear.

Name of person completing this form \_\_\_\_\_ Signature \_\_\_\_\_ Date (y/m/d) \_\_\_\_\_

# COMMERCIAL INVOICE

<b>DATE OF EXPORTATION</b>	<b>EXPORT REFERENCES</b>
<b>SHIPPER/EXPORTER</b>	<b>CONSIGNEE</b>  Kinexus Bioinformatics Corporation Suite 1 8755 Ash Street Vancouver, B.C. Canada V6P 6T3  Telephone: (604) 323-2547 Facsimile: (604) 232-2548 Email: info@kinexus.ca
<b>COUNTRY OF EXPORT</b>	<b>TERMS OF SALE</b> Not for resale, sample for analysis
<b>COUNTRY OF ORIGIN</b>	<b>PURPOSE</b> Research and development
<b>COUNTRY OF ULTIMATE DESTINATION</b> Canada	<b>EXPORTING CARRIER</b>
<b>INTERNATIONAL AIR WAYBILL NUMBER</b>	
Courier Name: _____ Number: _____	

NO. OF PKGS	TYPE OF PACKAGING	QUANTITY OF SAMPLES	COMPLETE AND ACCURATE COMMODITY DESCRIPTION	UNIT VALUE
	<input type="checkbox"/> FedEx Letter <input type="checkbox"/> FedEx Pak <input type="checkbox"/> Box <input type="checkbox"/> Other	<i>Total number of tubes and plates:</i>	Non-hazardous, cells and compounds for R&D development diagnostic purposes. Samples are not for resale and there is no commercial value.  Samples are packaged on Dry Ice, Class 9, UN 1845, Group 3 (____ X ____ kgs).	<b>\$1.00</b> <i>per sample</i>
<b>TOTAL NO. OF PACKAGES</b>		<b>TOTAL WEIGHT OF PACKAGES</b>		<b>TOTAL DECLARED VALUE</b>
				\$

*These commodities were exported from the Country indicated above in accordance with the Export Administration Regulations and are licensed for the ultimate designation shown. It is hereby certified that this commercial invoice shows the actual price of the goods described, that no other invoice has been or will be issued for these goods, and that all particulars are true and correct.*

**SIGNATURE AND STATUS OF AUTHORIZED PERSON**

Print Name	Title
Authorized Signature	Date (month/day/year)

INCLUDE THREE (3) COPIES OF THIS INVOICE WITH YOUR SHIPMENT



## PROTEOMICS SERVICES AGREEMENT

SERVICE AGREEMENT NO.

This Agreement is entered into effective as of the Effective Date by and between Kinexus Bioinformatics Corporation (“**Kinexus**”), a Canadian corporation with a principal place of business at Suite 1, 8755 Ash Street, Vancouver, British Columbia, Canada, V6P 6T3 **AND** the corporation or other entity (“**Customer**”) having the following name and business or institution address: \_\_\_\_\_

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### RECITALS

**WHEREAS** Kinexus is a bioinformatics company employing proprietary proteomics and bioinformatics services to create and interpret data to map protein signalling networks and compile databases with this knowledge to enable disease biomarker and therapeutics discovery.

**WHEREAS** the Customer desires to have Kinexus perform standard and/or customized proteomics services with materials and/or information provided by the Customer.

**WHEREAS** Kinexus is willing to provide these proteomics services under the terms and conditions set forth herein.

**THEREFORE**, in consideration of the premises and covenants and agreements contained herein, and other good and valuable consideration the receipt and sufficiency of which is hereby acknowledged, Kinexus and the Customer agree as follows:

#### 1. DEFINITIONS

1.1 "Academic Collaborator" means a principal investigator, employed at a university or other not-for-profit academic research institution.

1.2 "Affiliate" means any corporation or other entity that directly or indirectly controls, is controlled by or is under common control with a party to this Agreement. A corporation or other entity shall be regarded as in control of another corporation or entity if it owns or directly or indirectly controls more than fifty percent (50%) of the outstanding voting stock or other ownership interest of the other corporation or entity.

1.3 "Corporate Partner" means any Third Party which enters into an agreement with the Customer or its Affiliates involving the grant to such Third Party of rights for the development or commercialization of a product that was discovered, identified, selected, characterized or determined to have therapeutic or diagnostic use through use of the Proteomics Analyses provided to the Customer pursuant to this Agreement.

1.4 "Confidential Information" means any information or data received by a party (the “Receiving Party”) from the other party (the “Disclosing Party”) in connection with the performance of this Agreement that, if

disclosed in writing, is marked or otherwise identified by the Disclosing Party as confidential or, if disclosed orally is identified in writing by the Disclosing Party as confidential within ten (10) days following the disclosure. Confidential Information shall not include any information or data that the Receiving Party can demonstrate:

- (a) was generally available to the public before its disclosure to the Receiving Party or became generally available to the public after its disclosure to the Receiving Party, provided that such information or data did not become generally available to the public by means of an unauthorized act or omission of the Receiving Party;
- (b) was already in the possession of the Receiving Party before its disclosure under this Agreement, as demonstrated by Receiving Party's written records, provided that such information or data was not obtained directly or indirectly from the Disclosing Party under an obligation of confidentiality;
- (c) was disclosed to the Receiving Party, whether before or after its disclosure under this Agreement, by a Third Party, provided that such information or data was not obtained directly or indirectly from the Disclosing Party under an obligation of confidentiality; or
- (d) was independently developed or discovered by employees or agents of the Receiving Party without any use of Confidential Information of the Disclosing Party as demonstrated by Receiving Party's written records.

All of the Proteomics Services technologies provided by Kinexus will be deemed to have been identified as proprietary and considered the Confidential Information of Kinexus.

1.5 "Contact" means the contact person of the Customer that is designated on the Service Order Forms, who is deemed to have the authority to deliver Samples, Service Order Forms, Service Information Forms, and Sample Description Forms to Kinexus, on behalf of the Customer, under this Agreement.

1.6 "Proteomics Analyses" means one or more of the Custom and Standard Proteomics Services offered by Kinexus that may permit the identification and/or quantification of proteins, their phosphorylation states, their interactions with proteins, peptides, and other compounds, and the regulation of their functional activities by these agents.

1.7 "Proteomics Products" means the products of the Custom Proteomics Services offered by Kinexus to manufacture one or more proteins using recombinant DNA technology, and designer peptides by chemical synthesis.

1.8 "Sample" means a lysate or semi-purified fraction from cells and tissues, a protein, and/or a compound provided to Kinexus by the Customer, which the Customer has prepared and shipped in a manner that it can be properly used by Kinexus for the Proteomics Analyses. Samples for Proteomics Analyses may also be provided by Kinexus at the request of the Customer.

1.9 "Sample Description Form" means the Kinexus form to be completed by the Customer to provide information on the nature of each Sample submitted for the Proteomics Analyses. It is included in the Proteomics Services Customer Information Package with this Agreement, and may be amended from time to time as updated on the Kinexus website.

1.10 "Antibody" means the immunoglobulin reagent that permits detection of a target protein or phosphorylation site.

1.11 "Antibody Description Form" means the Kinexus form to be completed by the Customer to provide information on the nature of each Antibody submitted by the Customer for the Proteomics Analyses. It is included

in the Proteomics Services Customer Information Package with this Agreement, and may be amended from time to time as updated on the Kinexus website.

1.12 "Service Order Form" means the Kinexus form to be completed by the Customer to provide Kinexus with the Customer's contact and billing information for the Proteomics Analyses or Proteomics Products. This form indicates the level of confidentiality requested by the Customer. It is included in the Proteomics Services Customer Information Package with this Agreement, and may be amended from time to time as updated on the Kinexus website.

1.13 "Service Information Form" means the Kinexus form to be completed by the Customer to provide Kinexus with a specific listing of the Samples to be tested for the Proteomics Analysis or a specific description of the Proteomics Products that are requested. It is included in the Proteomics Services Customer Information Package with this Agreement, and may be amended from time to time as updated on the Kinexus website.

1.14 "Report" means the underlying raw data and the report provided to The Customer hereunder consisting of the Proteomic Analyses of Samples, including, but not limited to tables of the experimental results. For Proteomics Products, the Report may include raw data confirming the composition and purity of the Proteomics Products.

1.15 "Field of Use" means use by Kinexus and its Affiliates and Academic Collaborators of data from the Report for research and commercial purposes relating to the creation and interpretation of knowledge about the composition, architecture and operation of cell signalling networks, improving its Proteomics Services, and the compilation of databases that may become accessible to Third Parties on-line over the Internet.

1.16 "Third Party" means any entity other than Kinexus', Kinexus' Affiliates, the Customer and the Customer's Affiliates.

1.17 "Effective Date" means the date of the last signature on this Agreement.

## **2. REQUEST FOR AND DELIVERY OF PROTEOMICS SERVICES**

2.1 Request for Proteomics Services. From time to time, over the Term of this Agreement (as defined in Section 6.1 herein), the Customer can engage Kinexus to provide its Proteomics Analyses or Proteomics Products. After submission of a quotation from Kinexus to the Customer, by delivery to Kinexus of a Service Order Form, a Service Information Form and a Sample Description Form with Samples as appropriate, the Customer hereby requests and authorizes Kinexus to perform Proteomics Services and deliver the results of these services to the Customer, pursuant to the terms and conditions in this Agreement. In the case of Customer requested Proteomics Analyses, this would include the delivery of a Report. In the case of Customer requested Proteomics Products, this would include the delivery of the Proteomics Products and a Report.

2.2 Representation and Warranty. The Customer represents and warrants that: (a) it has all right and authority to provide the Sample to Kinexus for analysis under the terms and conditions of this Agreement, (b) it collected the Sample lawfully and with all necessary consents and approvals, and (c) that the collection, use and disclosure of the Sample by Kinexus pursuant to this Agreement will not violate the rights of any Third Party.

2.3 Delivery Conditions for Customer Sample. The Customer shall be responsible for making shipping arrangements to deliver Samples to Kinexus. The Customer shall also be responsible for complying with all applicable laws and regulations (including but not limited to customs requirements and relevant handling procedures and protocols) and obtaining any and all permits, forms or permissions that may be required by all regulatory authorities to ship and deliver the Sample; to Kinexus and for Kinexus to accept delivery of the Sample.

2.4 Processing and Delivery of Report and Proteomics Products. Subject to the terms of this Agreement, Kinexus shall analyze Samples with the Customer-specified Proteomics Services or produce Customer-specified Proteomics Products, and deliver a Report to the Customer as requested on the Service Order Form and Service Information Form.

2.5 Quality of Samples for Proteomics Analyses. Kinexus shall not deliver a Report on any Sample that Kinexus, in its sole discretion, believes has not been prepared and delivered in a manner that would compromise its ability to provide a reliable result. Under such a circumstance, the Sample will be destroyed by Kinexus after ten (10) days notification by e-mail to the Customer or at the request of the Customer prior to the scheduled destruction of the Sample, it will be returned to the Customer provided that the Customer agrees to reimburse Kinexus for the courier costs for its delivery.

### 3. PAYMENTS

3.1 Payments for Proteomics Services. For each Proteomics Analyses and Proteomics Product requested under this Agreement, the Customer shall pay to Kinexus a fee in accordance with the amount specified on the Service Order Form and the Service Identification Form for the requested service, which may be amended from time to time as updated on Kinexus' website. This amount will be based on a formal quotation issued by Kinexus to the Customer. In the absence of a formal quotation, the pricing will be based on the pricing specified in the latest versions of the Customer Information Packages for Proteomics Services that are downloadable from the Kinexus website ([www.kinexus.ca](http://www.kinexus.ca)). The category of pricing depends on the level of requested confidentiality for analysis:

- (a) Non-Confidential Analyses. If the Samples are provided by the Customer, then all of the Sample information on the Client Supplied **Non-Confidential** Sample Description Form is completed and **is not** designated as Confidential Information on the Service Identification Form. If Antibodies are supplied by the Customer, then all of the Antibody information on the Client Supplied Antibody Description Form (see example in Appendix) must be completed and **is not** designated as Confidential Information on the Service Identification Form.
- (b) Confidential Analyses. If the Samples are provided by the Customer, then all of the Sample information on the Client Supplied **Confidential** Sample Description Form must be completed and **is** designated as Confidential Information on the Service Identification Form.

3.2 The Customer shall issue a purchase order or provide a charge account at the time the Customer sample arrives at Kinexus' offices at Suite 1, 8755 Ash Street, Vancouver, British Columbia, Canada, V6P 6T3. Kinexus will invoice Customer when the Proteomics Analyses or Proteomics Products are complete and delivered to Customer. Payment terms are net 30 days from date of invoice.

3.3 Interest on Late Payments. Any overdue payments by the Customer to Kinexus under this Agreement shall bear interest, to the extent permitted by applicable law at 18% per annum, calculated on the total number of days payment is delinquent; provided, however, that interest shall not accrue pursuant to this Section 3.3 on any amounts payable under this Agreement with respect to which payment is disputed in good faith; provided, further that interest shall accrue pursuant to this Section 3.3 once such dispute has been resolved if payment is not made promptly thereafter.

## 4. INTELLECTUAL PROPERTY RIGHTS

4.1 Ownership of Sample Information. The Customer owns all rights to the Sample information provided to Kinexus. For Non-Confidential Proteomics Analyses, the Customer grants Kinexus a non-exclusive, royalty-free fully paid up worldwide perpetual license to use, copy, publish, compile, display, communicate, modify, translate and otherwise exploit (and authorize Third Parties to do any of the foregoing) to use the information on the Client Supplied **Non-Confidential** Sample Description Form in the Field of Use, provided that the Customer's identity is not linked to, or otherwise disclosed with respect to, such data.

4.2 Ownership of Report. The Customer shall own the data in the Report. For Non-Confidential Proteomics Analyses, the Customer grants Kinexus a non-exclusive, royalty-free fully paid up worldwide perpetual license to use, copy, publish, compile, display, communicate, modify, translate and otherwise exploit (and authorize Third Parties to do any of the foregoing) data from the Report in the Field of Use.

4.3 Confidentiality of Sample Information. Kinexus will have no rights with respect to the Confidential Sample information until the Sample information is published or otherwise enters the public domain. Thereafter, Kinexus can use the results of the Proteomics Analyses of the Customer Samples for its internal research and development programs.

4.4 Ownership of Proteomics Products. The Customer owns the Proteomics Products that have been delivered to the Customer in the amounts specified in the Service Order Form and the Service Information Form. Kinexus owns any excess Proteomics Products and may dispose of these in its best interests.

4.5 Ownership of New Intellectual Property.

- (a) The Customer shall own and have rights to all inventions, discoveries, improvements, know-how, technical information, data or other technology discovered, conceived, made, developed and/or reduced to practice through the use of the data in the Report and Proteomics Products solely by employees of the Customer or jointly with its Affiliates;
- (b) Kinexus shall own and have rights to all inventions, discoveries, improvements, know-how, technical information, data or other technology discovered, conceived, made, developed and/or reduced to practice through the use of the data in the Report and Proteomics Products solely by employees of Kinexus or jointly with its Affiliates.

4.6 Non-Exclusive License to Preserve Kinexus Proteomics Services Freedom of Operation. In the event one or more claims of an issued patent arising from the use of a Report by the Customer, its Affiliates, Academic Collaborators or Corporate Partners would, absent a license from the Customer or its Affiliates, prevent Kinexus from using or permitting others to use the Kinexus Proteomics Services or any data therein, then the Customer and/or its Affiliates (as applicable) shall grant to Kinexus a non-exclusive, royalty-free fully-paid up perpetual license, including the right to grant sublicenses, under any such patent claim to use and permit others to use the Proteomics Services.

## 5. CONFIDENTIALITY

5.1 Confidentiality. Each Receiving Party shall treat the Confidential Information of the Disclosing Party as strictly confidential and (a) take reasonable precautions to protect such Confidential Information (including, without limitation, all precautions such as the Receiving Party employs with respect to its own confidential information), (b) not disclose or make available to any Third Party such Confidential Information without the express prior written consent of the Disclosing Party and (c) use such Confidential Information only for purposes specifically authorized under this Agreement. Each Receiving Party may disclose Confidential



Information to its employees, consultants, Affiliates and agents, and to licensees or prospective licensees of its rights to any invention, on a need-to-know basis and on the condition that such employees, Affiliates, agents, licensees and prospective licensees are obligated to maintain the confidentiality of the Confidential Information under written agreements that contain terms and conditions no less restrictive than the terms and conditions of this Section 5. Each Receiving Party may disclose Confidential Information of the Disclosing Party pursuant to a demand issued by a court or governmental agency or as otherwise required by law, provided, however, that the Receiving Party notifies the Disclosing Party promptly upon receipt thereof, giving the Disclosing Party sufficient advance notice to permit it to seek a protective order or other similar order with respect to such Confidential Information, and provided, further, that the Receiving Party furnishes only that portion of the Confidential Information which it is advised by counsel is legally required whether or not a protective order or other similar order is obtained by the Disclosing Party.

5.2 Publication. The Customer may publish and/or present the Report, abstracts or manuscripts generated utilizing the Report, and any data and/or results generated by the Customer utilizing the Report. The Customer is encouraged to disclose in scientific publications any Proteomics Analyses that were performed by Kinexus and any Proteomics Products were produced by Kinexus that meaningfully contributed to the described work. Please refer to “Kinexus Bioinformatics Corporation (Vancouver, Canada).” For all Samples submitted for analysis and identified as Non-Confidential by the Customer, Kinexus will not use, copy, publish, compile, display, communicate, modify, or translate the Sample Information or the data from the Report for a period of 180 days (6 months) following the return of the Report to the Customer. At any time, the Customer may opt to pay the difference in price between the Non-Confidential pricing level to the Confidential pricing level for each applicable Sample, to ensure the confidentiality status of such sample is changed.

5.3 Confidential Sample Information. All parties agree that the term of confidentiality pertaining to that Sample information will expire when the Sample information is published or otherwise enters public domain through no fault of Kinexus.

5.4 Use of Customer Name. Except as expressly provided in Section 9.5, no right or license is granted hereunder by Customer for Kinexus to use the Customer’s name in relation to data from a Report to a third party.

## 6. TERM AND TERMINATION

6.1 Term. The term of this Agreement (“**Term**”) shall commence on the Effective Date and shall remain in effect for fifteen (15) years or until the termination of this Agreement pursuant to the terms hereof.

6.2 Early Termination. Each party shall have the right to terminate this Agreement at any time prior to Kinexus' delivery of a Report or Proteomics Product to the Customer hereunder, upon ten (10) days written notice to the other party, if such party reasonably determines that the production, or use of such Sample infringes intellectual property rights of any Third Party, and the Customer elects not to obtain a license under the necessary Third Party intellectual property rights at its sole expense. If this Agreement is terminated by either party pursuant to this Section 6.2, neither party shall have any obligation to the other with respect to payments under this Agreement regarding the Sample or Proteomics Product at issue.

Kinexus shall have the right to terminate any work order for any Proteomics Services upon ten (10) days written notice to the Customer, upon the identification of a technical difficulty related to the Sample or Proteomics Product which would prevent it from delivering the Report or Proteomics Product using reasonable efforts. If Kinexus terminates a work order as a result of a technical difficulty related to a Customer Sample that is the fault of Kinexus, Kinexus shall provide for the reanalysis of the same number of problematic Customer Samples for the Proteomics Analyses at the original agreed upon price without any additional expenses incurred by the Customer, or Kinexus shall repay any prepayment fee paid by the Customer for such a Customer Sample and neither party shall have any further obligation to the other with respect to that Customer Sample.

If Kinexus terminates a work order for Proteomics Analyses as a result of a technical difficulty related to the Customer Sample (including insufficient material or other problems associated with the quality of the Sample) that is the fault of the Customer, then Kinexus shall provide for the reanalysis of the problematic Customer Samples at the original agreed upon price without any additional expenses incurred by the Customer, provided Kinexus completes the full Proteomics Analyses for all Samples. For any subsequent resubmission of Customer Samples for Proteomics Analyses due to technical difficulty that is again the fault of the Customer, Kinexus shall provide for the reanalysis of the problematic Customer Samples at an additional charge per sample at a price mutually agreed by the Customer and Kinexus. If the Customer elects not to resubmit Samples for Proteomics Analyses, then the Customer will pay Kinexus an amount equivalent to 50% of the quoted price for the work performed by Kinexus to this point.

6.3 Events of Default. An event of default (an “Event of Default”) shall be deemed to occur upon a material breach of this Agreement by a party (including, without limitation, any breach of the provisions of Section 5) if the breaching party fails to remedy such breach within thirty (30) days after written notice thereof by the non-breaching party.

6.4 Effect of an Event of Default.

- (a) Remedies Available to Kinexus. If an Event of Default occurs relating to a material breach by the Customer, then Kinexus shall have the right, at its option exercisable in its sole discretion, in addition to any other rights or remedies available to it at law or in equity, to immediately terminate this Agreement upon notice thereof to the Customer, in which case the Customer shall return to Kinexus, or, upon Kinexus' written instruction, destroy any Report, Proteomics Products, and all information, other materials or documentation provided or made available by Kinexus pursuant to this Agreement, and any copies thereof (including electronic copies).
- (b) Remedies Available to the Customer. If an Event of Default occurs relating to a material breach by Kinexus, then the Customer shall have the right, at its option exercisable in its sole discretion, in addition to any other rights or remedies available to it at law or in equity and subject to the limitations set forth in Section 7, to terminate this Agreement upon notice thereof to Kinexus.

6.5 Effect of Expiration or Termination of Agreement. The expiration or termination of this Agreement shall not relieve the parties of any obligation accruing prior to such expiration or termination. Kinexus will not be required to continue Custom Immunohistochemistry Analyses on a Sample after termination, and the Customer will be required to pay for work done prior to termination. The provisions of Sections 4, 5, 6, 7, 8, and 9 hereof shall survive any expiration or termination of this Agreement.

## **7. DISCLAIMER OF WARRANTIES AND LIMITATION OF LIABILITY**

7.1 Disclaimer of Warranties. THE PROTEOMICS SERVICES ARE BEING SUPPLIED TO CUSTOMER WITH NO EXPRESS, IMPLIED, STATUTORY OR OTHER WARRANTIES, REPRESENTATIONS, CONDITIONS OR GUARANTEES, INCLUDING THOSE OF MERCHANTABILITY, FITNESS FOR A PARTICULAR PURPOSE, TITLE AND DURABILITY. WITHOUT LIMITING THE FOREGOING, KINEXUS MAKES NO REPRESENTATION OR WARRANTY THAT THE USE OF THE REPORT, ANY PROTEOMICS PRODUCTS OR THE DATA THEREIN OR THE PERFORMANCE OF THIS AGREEMENT WILL NOT INFRINGE ANY INTELLECTUAL PROPERTY OR OTHER RIGHTS OF ANY THIRD PARTY.

7.2 Limitation of Liability. Kinexus shall not be liable for any use by the Customer, its Affiliates, Corporate Partners, or Academic Collaborators of the Report and any Proteomics Products or any loss, claim,

damage or liability, of whatever kind or nature, which may arise from or in connection with the use of the Report or the data therein, and any Proteomics Products. NOTWITHSTANDING ANYTHING ELSE IN THIS AGREEMENT OR OTHERWISE TO THE CONTRARY, NEITHER KINEXUS NOR CUSTOMER WILL BE LIABLE TO EACH OTHER WITH RESPECT TO ANY MATTER ARISING UNDER THIS AGREEMENT UNDER ANY CONTRACT, NEGLIGENCE, STRICT LIABILITY OR OTHER LEGAL OR EQUITABLE THEORY FOR (I) ANY PUNITIVE, EXEMPLARY, INCIDENTAL OR CONSEQUENTIAL DAMAGES OR LOST PROFITS OR (II) COST OF PROCUREMENT OF SUBSTITUTE GOODS, TECHNOLOGY OR SERVICES. WITHOUT IN ANY WAY LIMITING THE FOREGOING, KINEXUS SHALL NOT, IN ANY EVENT, HAVE ANY LIABILITY WHATSOEVER IN CONNECTION WITH THIS AGREEMENT IN EXCESS OF AN AMOUNT EQUAL TO THE FEES PAID TO KINEXUS BY CUSTOMER HEREUNDER IN RESPECT OF THE PROTEOMICS SERVICES AT ISSUE.

## 8. INDEMNIFICATION

Except to the extent prohibited by law, the Customer shall assume all liability for, and shall defend, indemnify and hold Kinexus, its Affiliates and their respective directors, officers, employees and agents harmless from, all claims, losses, damages or expenses (including reasonable attorneys' fees) arising directly or indirectly as a result of: (a) the use of the Report or the data therein and any Proteomics Products by the Customer or its Affiliates, Corporate Partners or Academic Collaborators, or (b) the breach, untruthfulness or inaccuracy of any of the Customer's representations and warranties in this Agreement.

## 9. MISCELLANEOUS

9.1 Entire Agreement. The Appendices to this Agreement, together with all terms and conditions contained within this Agreement constitute the entire understanding between the parties with respect to the subject matter hereof and, with respect to any conflicting terms from prior agreements between the parties, supersedes and cancels such conflicting sections from all previous registrations, agreements, commitments and writings in respect thereof. This Agreement may be amended, or any term hereof modified, only by a written instrument duly executed by both parties hereto.

9.2 Assignment and Waiver. This Agreement may not be assigned or otherwise transferred by either party without the written consent of the other party, such consent will not be unreasonably withheld. Notwithstanding the foregoing, Kinexus may, without such consent, assign its rights and obligations under this Agreement (a) to any Affiliate or (b) to a Third Party in connection with a merger, consolidation or sale of such portion of its assets that includes rights under this Agreement provided, however, that Kinexus' rights and obligations under this Agreement shall be assumed by its successor in interest in any such transaction. In the event of such a transaction with Third Party, notwithstanding the other provisions of this Agreement, the intellectual property rights of such Third Party shall not be subject to the licenses granted by Kinexus under this Agreement. Any purported assignment in violation of the provisions of this Section 9.2 shall be void. Any permitted assignee shall assume all obligations of its assignor under this Agreement. The waiver by either party hereto of any right hereunder or the failure to perform or of a breach by the other party shall not be deemed a waiver of any other right hereunder or of any other breach or failure by said other party whether of a similar nature or otherwise.

9.3 Force Majeure. Neither party shall be held liable or responsible to the other party nor be deemed to have defaulted under or breached this Agreement for failure or delay in fulfilling or performing any obligation under this Agreement when such failure or delay is caused by or results from causes beyond the reasonable control of the affected party, including but not limited to fire, floods, embargoes, war, acts of war (whether war is declared or not), insurrections, riots, civil commotions, strikes, lockouts or other labor or supply disturbances, acts of God or acts, omissions or delays in acting by any governmental authority or the other party; provided, however, that the party so affected shall use reasonable commercial efforts to avoid or remove such causes of nonperformance, and

shall continue performance hereunder with reasonable dispatch whenever such causes are removed. Either party shall provide the other party with prompt written notice of any delay or failure to perform that occurs by reason of force majeure. The parties shall mutually seek a resolution of the delay or the failure to perform as noted above.

9.4 Notices. Any consent, notice, or report required or permitted to be given or made under this Agreement by one of the notification parties hereto to the other shall be in writing, delivered personally, by email or by facsimile (and promptly confirmed by telephone, personal delivery or courier) or courier, postage prepaid (where applicable), addressed to such other party at its address indicated below, or to such other address as the addressee shall have last furnished in writing to the addressor and shall be effective upon receipt by the addressee.

*If to Kinexus:*

Kinexus Bioinformatics Corporation  
Suite 1, 8755 Ash Street  
Vancouver, British Columbia, Canada V6P 6T3  
Attention: Dr. Steven Pelech  
President & C.S.O.  
Telephone: (604) 323-2547 extension 10  
Facsimile: (604) 323-2548

*If to the Customer:*

To the Customer at the address designated at the front of this Agreement and to the attention of the duly authorized representative signing this Agreement.

9.5 Publicity. Except as required by law, the terms of this Agreement shall be treated as Confidential Information and shall not be disclosed to anyone (except for the parties' respective directors, officers, employees, consultants, agents and attorneys assisting in the review and negotiation of this Agreement and/or who have a need to know the terms of this Agreement) without the written consent of the other party, such consent which will not be unreasonably withheld. Notwithstanding the foregoing, (a) Kinexus may, without such consent, publicly announce the execution of this Agreement with the Customer and may reference the Customer as a Kinexus client.

9.6 No Partnership. It is expressly agreed that the relationship between Kinexus and the Customer shall not constitute a partnership, joint venture or agency. Neither Kinexus nor the Customer shall have the authority to make any statements, representations or commitments of any kind, or to take any action, which shall be binding on the other, without the prior consent of the other party to do so.

9.7 Applicable Law. This Agreement shall be governed by, construed, interpreted and enforced in accordance with, the laws of the province of British Columbia and the laws of Canada, without reference to conflict of laws principles.

9.8 Dispute Resolution.

- (a) The parties hereby agree that they will attempt in good faith to resolve any controversy or claim arising out of or relating to this Agreement promptly by negotiations. If a controversy or claim should arise hereunder, the matter shall be referred to an individual designated by the Chief Executive Officer or President of Kinexus and an individual designated by the Chief Executive Officer (or the equivalent position) of the Customer (the "Representatives"). If the matter has not been resolved within twenty-one (21) days of the first meeting of the Representatives of the parties (which period may be extended by mutual agreement) concerning such matter, subject to rights to injunctive relief and specific performance, and unless otherwise specifically provided for herein, any controversy or claim arising out of or relating to this Agreement, or the breach thereof, will be settled as set forth in Section 9.8(b).

- (b) All disputes arising in connection with this Agreement that are not resolved pursuant to Section 9.8(a) above shall be finally settled in Vancouver, British Columbia, by a single arbitrator appointed pursuant to the provisions of the *Commercial Arbitration Act* (British Columbia). Notwithstanding the above, either party has the right to bring an action in a court of competent jurisdiction against the other party for (i) any breach of such other party's duties of confidentiality pursuant to Section 5 of this Agreement; (ii) any infringement of its proprietary rights by the other party; and (iii) for interim protection such as, by way of example, an interim injunction. Judgment upon the arbitrator's award may be entered in any court of competent jurisdiction. The award of the arbitrator may include compensatory damages against either party, but under no circumstances will the arbitrator be authorized to, nor shall he/she, award punitive, consequential or incidental damages against either party. The parties agree not to institute any litigation or proceedings against each other in connection with this Agreement except as provided in this Section 9.8.

9.9 Severability. Each party hereby agrees that it does not intend to violate any public policy, statutory or common laws, rules, regulations, treaty or decision of any government agency or executive body thereof of any country or community or association of countries. Should one or more provisions of this Agreement be or become invalid, the parties hereto shall substitute, by mutual consent, valid provisions for such invalid provisions which valid provisions in their economic effect are sufficiently similar to the invalid provisions that it can be reasonably assumed that the parties would have entered into this Agreement with such valid provisions. In case such valid provisions cannot be agreed upon, the invalidity of one or several provisions of this Agreement shall not affect the validity of this Agreement as a whole, unless the invalid provisions are of such essential importance to this Agreement that it is to be reasonably assumed that the parties would not have entered into this Agreement without the invalid provisions.

9.10 Counterparts. This Agreement may be executed in counterparts, each of which when executed and delivered is an original, but both of which together shall constitute one and the same instrument.

9.11 Fax Delivery. This Agreement may be executed by the parties and transmitted by facsimile and if so executed and transmitted this Agreement will be for all purposes as effective as if the parties had delivered an executed original Agreement.

**IN WITNESS WHEREOF**, the parties have caused their duly authorized officer to execute and deliver this Agreement as of the Effective Date.

\_\_\_\_\_  
*Printed Name of Institute or Company*

Per: \_\_\_\_\_  
*Signature of Authorized Representative*

Name: \_\_\_\_\_  
*Printed Name of Authorized Representative*

Title: \_\_\_\_\_  
*Printed Title of Authorized Representative*

Date signed: \_\_\_\_\_

**KINEXUS BIOINFORMATICS CORPORATION**

Per: \_\_\_\_\_  
*Signature of Dr. Steven Pelech*

**Dr. Steven Pelech**

**President and Chief Scientific Officer**

Date signed: \_\_\_\_\_