

**MASS
SPECTROMETRY
SERVICES
PIMS**
Version 10NO11

MASS SPEC SERVICES

**PROTEIN ID BY MASS SPECTROMETRY
CUSTOMER INFORMATION PACKAGE**

For identification of antibody
cross-reactive proteins detected
by immunoblotting.

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

Facsimile: 604-323-2548

E-mail: info@kinexus.ca

www.kinexus.ca

KINEXUS



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KINEXUS PROTEIN IDENTIFICATION BY MASS SPECTROMETRY SERVICE

1. INTRODUCTION

General Methodology

Protein identification by mass spectrometry (PIMS) 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 several species such as 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

Our PIMS Service is positioned relative to the other services offered by Kinexus as a follow on supplement to our core Kinex™ antibody microarray (KAM) and Kinetworks™ multi-immunoblotting services, and is a means of obtaining additional information from these early stage protein profiling services. These initial stage services utilize Kinexus' unique antibody microarrays and multi-immunoblots to track the differential binding of proteins in lysates prepared from cells and tissues. The results can provide some valuable antibody information relating to differences in protein expression, phosphorylation and protein-protein interactions, but due to the ability of antibodies to cross-react with non-target proteins, this information is not always sufficient to positively link an antibody to the protein. Our PIMS service can establish a positive link, and allow follow-up studies to validate an interesting protein biomarker in larger numbers of biological specimens.

Protein Identification by Mass Spectrometry is carried out by immunoprecipitation of the protein of interest using an antibody identified in the KAM or subsequent Kinetworks™ multi-immunoblotting services. Then, the immunoprecipitate is subjected to SDS-polyacrylamide gel electrophoresis (SDS-PAGE) to resolve a novel-sized protein, meaning a protein different in size from the expected antibody target. The protein band of interest is then excised from the SDS-PAGE gel, subjected to trypsin digestion to produce a characteristic set of tryptic peptide fragments, and then analyzed by high-resolution mass spectrometry to determine their accurate masses. A search of the appropriate protein sequence databases using a Mascot search (www.matrixscience.com) for a matching mass pattern can then lead to a definitive identification of the protein. The mass spectrometry is performed on an LC-MS/MS using a Thermo Electron LTQ-Orbitrap.

The methodology of the protein identification process is described in the following two figures. Figure 1 illustrates an experimental design using untreated versus treated cells or tissues. The untreated arm is an important control for identifying protein bands that respond to treatment (and may be potential biomarkers). Figure 2 illustrates an alternative design where untreated control cells or tissues may not be available in sufficient quantities. In this case, the agarose beads without conjugated antibody are used as a negative control for immunoprecipitation. This allows the differentiation between protein bands that bind nonspecifically to the beads, versus proteins that bind specifically to the antibody.

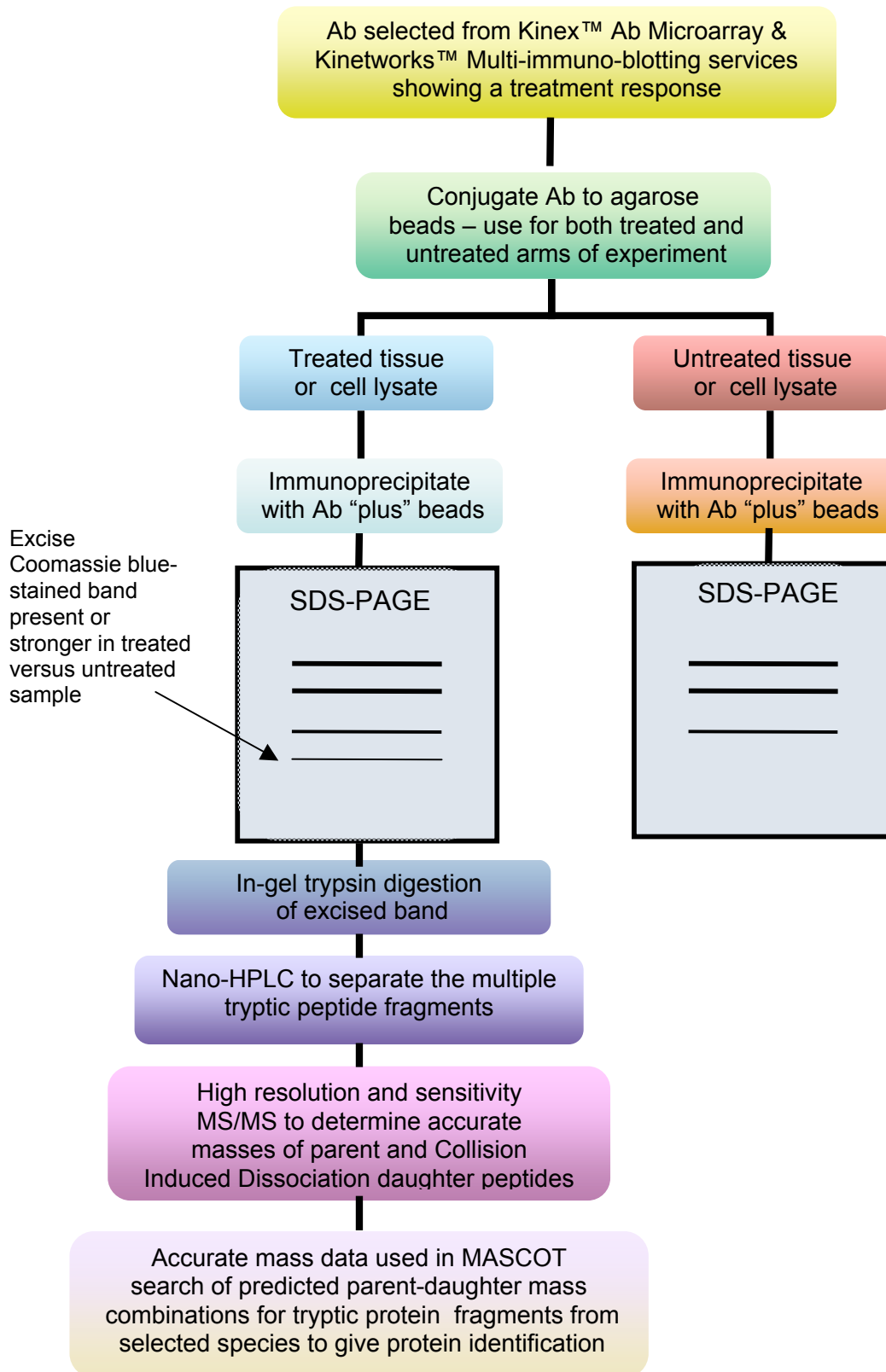


Figure 1. Methodology of protein identification by mass spectrometry using untreated cells in the negative control arm.

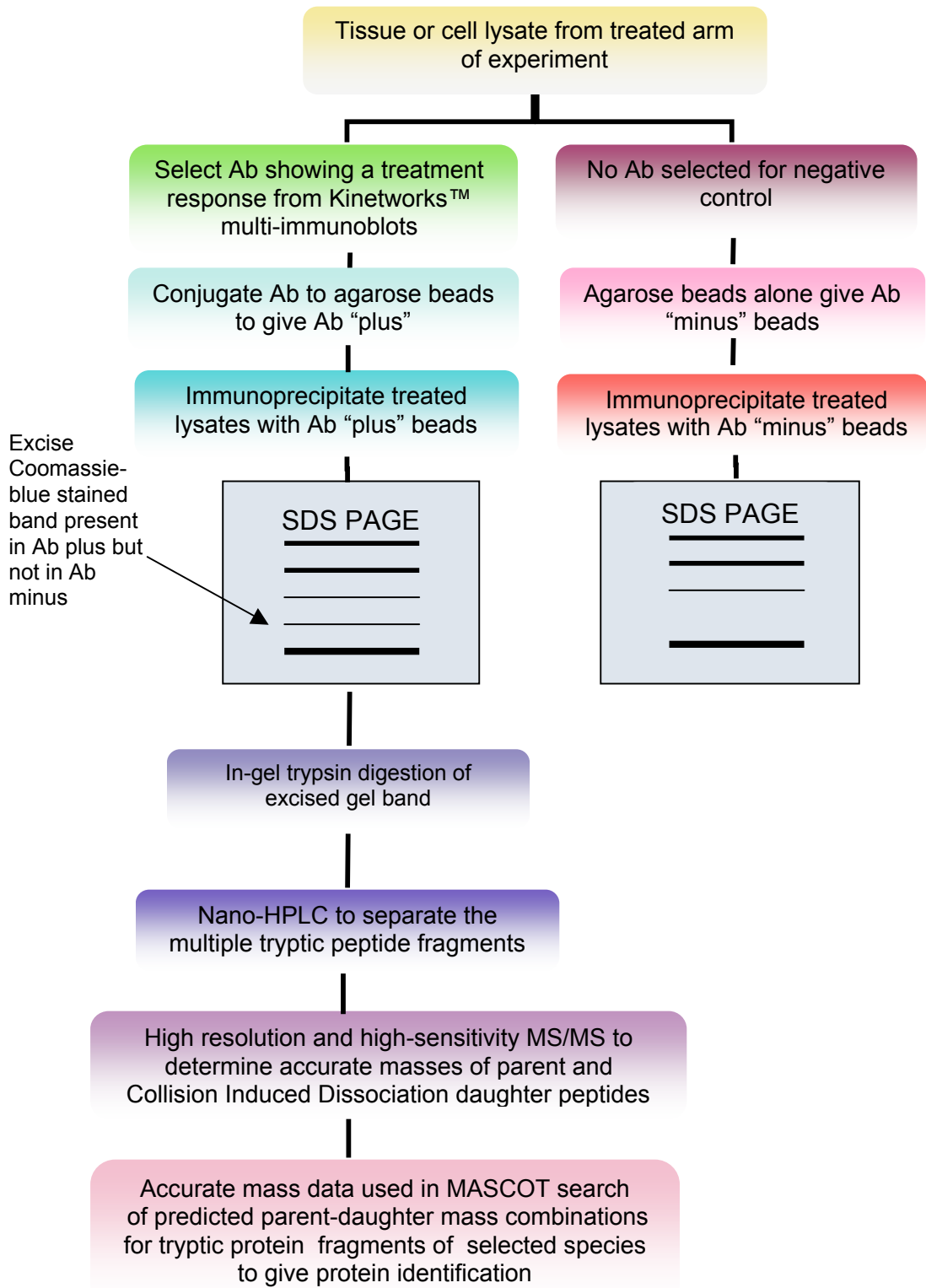


Figure 2. Methodology of protein identification by mass spectrometry using agarose beads without antibody as a negative control.

Example Study – Effects of a Compound on Protein Expression in Rat Lung

A company studying the effects of a compound on lung function carried out a study where laboratory rats were subjected to the agent and then the lung tissue was analyzed using the Kinex™ antibody microarray service. Several antibodies were identified to recognize proteins that were elevated in the agent treated group versus the untreated control group. Four of these antibodies were selected to be subjected to our PIMS service..

Each antibody was conjugated to agarose beads and incubated with 4 mg of rat lung lysate protein from the compound-treated animals to immunoprecipitate the protein(s) that were potential biomarkers. The control used in this test was the agarose beads without antibody.

Out of the 4 antibodies used for immunoprecipitation, there were two that revealed one or more gel bands in the antibody plus immunoprecipitate versus the antibody minus samples. The differentially affected bands were excised and subjected to trypsin digestion and LC-MS/MS. One of these could be identified with high confidence in a Mascot search.

The above example study illustrates some caveats with respect to the performance and success rate of the Kinexus PIMS Service. Firstly, an antibody identified in the Kinex™ antibody microarray, even if it is confirmed in the follow-up Kinetworks™ multi-immunoblots will not necessarily succeed in immunoprecipitating a differentially expressed protein band visible on a Coomassie blue-stained gel. The antibody microarray or immunoblot methods are much more sensitive than a Coomassie blue-stained gel, so it is possible that the immunoprecipitated protein is present below the detection limit of Coomassie blue. Secondly, when a Coomassie blue-stained protein band is visible as a differentially expressed protein, the identification by mass spectrometry does not always yield a high probability identification. Peptide masses be influenced, for example, by phosphorylation of the protein or a variety of other covalent modifications. Factors such as small tryptic peptide size and poor reverse-phase LC resolution will affect the degree of certainty for a given mass spectrometry protein identification. However, knowledge of the apparent molecular mass of the protein improves the likelihood of a correct identification.

A large body of information and instruction is provided with this PIMS 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/tissue lysate samples so that we may share with other scientists in the future. For these rights, we have discounted our standard charges by ~40% with our Non-Confidential Pricing option. You should find that the proper entry of information into the various forms provided by Kinexus will also be useful for your own reference at a later date when you receive your PIMS 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

2. TISSUE PREPARATION

Lysis Procedure

1. Keep tissue on ice at all times. Rinse whole uncut samples with ice cold PBS to remove surface blood, and then cut into pieces less than 1 mm in size.
2. Carry out lysis procedure in batches using 0.5 mL of lysis buffer for approximately 125 mg wet weight of chopped tissue contained in a 2 mL microfuge tube.
3. Homogenize tissue in lysis buffer on ice for 6 intervals of 10 seconds each, pausing 10 seconds between, using an ultrasonic probe (Vibracell, Sonics & Materials Inc. Danbury CT, USA, 40 Watt output generator or equivalent) with a 1.3 cm horn and 3 mm tip, at a power output setting of about 10 Watts
4. Centrifuge homogenate at 90,000 to 110,000 x g for 30 min at 4°C in a Sorvall M120 Micro-Ultracentrifuge (55,000 rpm using rotor S120-AT2 or equivalent).
5. Transfer the resulting supernatant fraction to a new tube and carry out a protein assay. Using a commercial Bradford assay (available from Bio-Rad, catalogue number 500-0201) or using the standard protocol of Bradford (*Bradford, M.M. (1976) A rapid and sensitive method for quantitation of microgram quantities of protein utilizing the principle of protein-dye binding Anal. Biochem. 72:248-254*). Bovine serum albumin should be used as the protein standard.

3. CELL AND TISSUE LYSATES

For the Protein Identification by Mass Spectrometry (PIMS) the preferred amount of lysate protein is 5 to 10 mg per sample submitted for immunoprecipitation at a concentration of 10 to 50 mg/mL. If this is not possible, then smaller amounts can be handled using modified procedures, but with lower probability of success. The samples must be frozen and shipped to Kinexus on dry ice fresh after protein quantification **WITHOUT ANY SDS-PAGE SAMPLE BUFFER** as the proteins are to remain in their native structure and nondenatured.

Important general points to remember are that the cells or tissues should be processed quickly at 4°C or less. Homogenization should not be performed in too large a volume to obtain lysates at the concentration required. The detergent-soluble fraction should be obtained as quickly as possible after the cells or tissues are homogenized. Sonication is required and cannot be omitted. The highest centrifugal forces available should be used to generate the detergent-soluble fraction. The supernatants should be frozen as quickly as possible if a protein assay cannot be performed immediately.

Standard Lysis Buffer

1. 20 mM MOPS, pH 7.0 adjusted using either 1 M HCl or 1 M NaOH (other pH buffering agents and be used as long as they do not contain reactive amine groups; TRIS cannot be used.);
2. 2 mM EGTA, pH 8.0 (to bind calcium);
3. 5 mM EDTA , pH 8.0 (to bind magnesium and manganese);
4. 30 mM sodium fluoride (to inhibit protein-serine phosphatases);
5. 60 mM beta-glycerophosphate, pH 7.2 (to inhibit protein-serine phosphatases);

6. 20 mM sodium pyrophosphate (to inhibit protein-serine phosphatases);
7. 1 mM sodium orthovanadate (to inhibit protein-tyrosine phosphatases);
8. 1% Triton X-100 (nonionic detergent to disrupt cellular membranes; 1% Triton X-100 can be substituted with 1% Nonidet P-40; Note: *Do not add detergent if you intend to first prepare a subcellular fraction*).

9. 1 mM phenylmethylsulfonylfluoride (to inhibit proteases);
10. 3 mM benzamidine (to inhibit proteases);
11. 5 μ M pepstatin A (to inhibit proteases);
12. 10 μ M leupeptin (to inhibit proteases);
13. 1 mM dithiothreitol (reducing agent to disrupt disulfate bonds, this concentration can be modified, depending upon objectives of experiment).

Note 1: The protease inhibitors phenylmethylsulfonylfluoride, benzamidine, pepstatin A leupeptin and the reducing agent *dithiothreitol* must be added to lysis buffer immediately before use. For convenience, one may choose to use the Roche Complete Protease Inhibitor Cocktail Tablet, Mini catalog# 04693124 in place of individual protease inhibitors. *The lysis buffer must be used ice-cold.*

Note 2: Other lysis buffers commonly used for protein lysate preparation with non-ionic detergents should still be compatible with the service. Please contact a Kinexus Technical Sales Representative for more information on the appropriate types of lysis buffers to use for the PIMS Service or to request to have an aliquot of our lysis buffer for free if you can provide a courier account number to charge for the shipping costs. Our lysis buffer contains components 1-8, including phosphatase inhibitors (components 4-7) and 1% Triton X-100 but *no protease inhibitors or dithiothreitol.*

Subcellular Fractions

Depending upon required cellular fraction, it may be required to modify the lysis buffer.

Total cellular fractionation: For quantitation of total cellular levels of cell signaling proteins, lysis and homogenization should be performed in the presence of a non-ionic detergent. We recommend the use of 1% Triton X-100 or 1% Nonidet P40, but comparable detergents are acceptable.

Subcellular fractionation: Detergents should be omitted from the homogenization buffer if the subcellular distribution of cell signalling proteins is to be examined. If a particulate-solubilized fraction is to be analyzed, a microsomal pellet should be obtained following the initial homogenization and ultracentrifugation in the absence of detergent and subsequent removal of the cytosolic supernatant. In this instance, the cytosolic extract should be removed and the microsomal pellet should then be resuspended in the homogenization buffer containing 1% Triton X-100 or 1% Nonidet P-40 and subjected to homogenization and ultracentrifugation once again. The resulting detergent-solubilized microsomal fraction should be removed and immediately assayed for its protein concentration.

4. PREPARATION OF CULTURED CELL LYSATES

A. Adherent Cell Lysates

1. From culture dishes containing a total minimum of 5×10^7 cells; remove the medium by aspiration.
2. Rinse the cells twice with ice-cold PBS to remove serum proteins from the cells after the last rinse, remove as much PBS as possible by aspiration. For sensitive cells, the rinses can be done medium without serum proteins.
3. Add 200 μ L ice-cold lysis buffer to 150 mm culture dish per sample (more lysis buffer can be added if cells are concentrated); (add 100 μ L ice-cold lysis buffer to 100 mm culture dish)
4. Scrape the cells in lysis buffer, collect the cell suspension from the dishes and transfer it into a 1.5-mL microcentrifuge tube;
5. Sonicate on ice to rupture the cells and to shear nuclear DNA; A typical sonication would be for 6 intervals of 10 seconds each, pausing 10 seconds between, using an ultrasonic probe with a 1/8th inch or 3 mm tip and power setting equivalent to about 10 Watts output (Vibracell VC40, Sonics & Materials Inc. Danbury CT, USA, 20 KHz 40 Watt maximum output generator or equivalent). **This step is crucial and cannot be omitted;**
6. Centrifuge the homogenate at 90,000 to 110,000 x g for 30 min at 4°C in a Sorvall M120 Micro-Ultracentrifuge (55,000 rpm using rotor S120-AT2 or equivalent);
7. Transfer the resulting supernatant fraction to a 1.5-mL microcentrifuge tube;
8. Assay sample for protein concentration using a commercial Bradford assay reagent (available from Bio-Rad, catalogue number 500-0201) or using the standard protocol of Bradford (*Bradford, M.M. (1976) A rapid and sensitive method for quantitation of microgram quantities of protein utilizing the principle of protein-dye binding. Anal. Biochem. 72:248-254*). Bovine serum albumin should be used as the protein standard.

B. Suspended Cell Lysates

1. Place medium containing cells in appropriate sized tube and centrifuge at 500 x g for 2 minutes at 4°C in a swinging bucket benchtop centrifuge. Remove as much medium from the cell pellet as possible without disrupting cells;
2. Wash the pellet by gently resuspending the cells in ice-cold PBS, followed by centrifugation as above. Repeat once to ensure complete removal of serum;
3. Remove as much PBS as possible after the last wash;
4. Add an adequate amount of ice-cold lysis buffer to the sample (more lysis buffer can be added if the number of cells is high);
5. Follow the procedure for adherent cells from step 5.

5. PREPARATION OF CELL PELLETS

An additional charge of \$200 per sample will apply for submission of cell pellets to be processed at Kinexus. Please submit a sufficient number of cells ($>5 \times 10^7$ cells) for processing.

A. Adherent Cells

1. Remove the medium and rinse the cells in dish with ice-cold PBS once;

2. Detach cells with trypsin as one does in passaging cells, followed by the addition of equal volume of medium;
3. Collect cells in a 15-mL conical tube and centrifuge at 500 x g for 2 minutes at 4°C in a swinging bucket benchtop centrifuge;
4. Wash the pellet twice with ice-cold PBS thoroughly, (the presence of serum from medium could skew the protein assay) and remove as much PBS as possible (the presence of liquid residue dilutes the sample and may also result in the damage of cells during freezing process);
5. Freeze the pellet for shipping. Pellet must be shipped on dry ice.

B. Suspended Cells

Simply follow steps 3-5 in Section 4A for “*for adherent cells*” and freeze the cell pellet immediately. Pellet must be shipped on dry ice.

SHIPPING AND PRICING

6. PREPARATION FOR STORAGE AND SHIPPING OF SAMPLES

For the Protein Identification by Mass Spectrometry (PIMS) the preferred amount of protein is 4 to 10 mg per sample submitted for immunoprecipitation at a concentration of 10 to 50 mg/mL. If this is not possible, then smaller amounts can be handled using modified procedures, but with lower probability of success. Please record the actual concentration and volume of each sample on the Sample Description Form (NSDF-LY or CSDF-LY). Samples should be stored in *screw cap* vials. The vials should be clearly labeled with an indelible marker with a unique identification number (recorded in the Sample Description Form), parafilmed, and then put into another support structure such as a 50-mL conical or centrifuge tube to provide extra protection during shipping. **All 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.

7. 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:

Protein Identification by Mass Spectrometry Services
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

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 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 confirmatory e-mail once your shipment arrives at our facility.

8. PRICING INFORMATION

Kinexus offers its services at different pricing levels depending on the level of confidentiality required for your samples and whether you are following on from a previous proteomics analysis with our Kinex™ and/or Kinetworks™ services. With our full Confidential option, our regular price starts at US \$750 per antibody immunoprecipitation and \$960 per protein gel slice analyzed by mass spectrometry. At this pricing level, only the species identity needs to be disclosed. With our Non-confidential option, clients can receive a 33% discount on the mass spectrometry analysis price. To receive the 33% discount, Kinexus requires the Client-Supplied Non-Confidential Sample Description Form (NSDF-LY) to be completed in full (Sections A-K) including species, organ, tissue, cell, cell state, fractionation, perturbation, and treatment for each sample being analyzed. Furthermore, if the work is a follow on from previous proteomics studies performed by Kinexus, we offer an additional 20% discount from the Confidential and Non-confidential prices.

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.

FOLLOW UP SERVICES AND FORMS

9. FOLLOW UP SERVICES

After an immuno-reactive protein with a phospho-site antibody has been identified with our PIMS services, clients may desire to identify the phosphorylation sites and the protein kinases that may target these phospho-sites. Kinexus can produce recombinant forms of the immuno-reactive protein or synthesize short peptides that are predicted from the amino acid sequence of the immuno-reactive protein. Using our proprietary Kinase and Phospho-site Predictor algorithms, Kinexus can identify known and putative phospho-sites and the kinases responsible for their phosphorylation. We can test these predictions 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 our custom proteomics services or visit our website at www.kinexus.ca.

10. FORMS TO BE COMPLETED

All of the forms necessary to use the Protein Identification by Mass Spectrometry (PIMS) services are provided in the Appendices section of this Customer Information Package. Fillable MS-Word versions of some of these forms may be obtained by request by e-mail or by phone or directly downloadable from the Kinexus website at <http://www.kinexus.ca/ourServices/massspectrometry/massspectrometry/proteinid.html>. Please contact our Technical Service Representatives by e-mail at 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.

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 (PIMS-SOF). The Service Order Form allows us to track all of the various services to be used within an order.
- C. Service Identification Form (PIMS-SIF). The Service Identification Form permits us to determine which proteomics service screen is to be used for the analysis of two cell/tissue lysate samples together.
- D. Sample Description Forms – Customers should choose one or both of the following forms that is applicable: Non-Confidential Sample Description Form (NSDF-LY); Confidential Sample Description Form (CSDF-LY). The Sample Description Forms (SDF's) allow us to determine the nature of the cell/tissue lysates to be analyzed. One SDF is completed per cell/tissue lysate sample. If clients wish to provide their own antibodies for immunoprecipitation, they should also complete either Non-Confidential Sample Description Forms (NSDF-AB) or Confidential Sample Description Forms (CSDF-AB) as applicable with information of these antibodies.
- E. Federal Express Airway Bill (if samples are to be delivered by courier).
- F. Commercial Invoice (required for all customers located outside of Canada).

All orders should have as a minimum: 1 SOF, 1 SIF, and 2 SDF forms completed, along with a courier airway bill and commercial invoice. 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

FOR ALL CUSTOMERS

A. Kinexus Service 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 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 (PIMS-SOF)

Please ensure:

- Shipping address and contact name and numbers are specified
- Billing information is completed as outlined in Section D on the Service Identification Form (PIMS-SIF)
- Any promotional vouchers or quotations are listed in the billing sections
- Include a Purchase Order, Visa or MasterCard number for payment
- The form is signed and dated

C. Service Identification Form (PIMS-SIF)

For each sample submitted, please ensure the following:

- In Section A, the customer must assign a unique Client Screen Identification Name to correlate the proteins to be analyzed for each sample submitted
- In Section B, the type of analysis (Kinex™ Screen Name) for each sample is specified.
- For Section C, your sample(s) are identified by completion of Client Supplied Non-Confidential (NSDF-LY) or Confidential (CSDF-LY) Sample Description Forms. Make sure that the Client Screen ID Name in Box A of these forms, matched the Client Screen ID Name in Box A of the PIMS-SIF form
- In Section D, the level of confidentiality is indicated for correct pricing
- The form is certified correct and signed and dated

D. Sample Description Forms

Client-Supplied Non-confidential Sample Description Form for Lysates (NSDF-LY)

Client-Supplied Confidential Sample Description Form for Lysates (CSDF-LY)

For the cell/tissue lysate samples submitted, please ensure the following:

- Each sample tube is labeled and properly identified on the form in Section B, including final concentration and volume
- Your sample is described by completion of Client-Supplied Non-Confidential (NSDF-LY) or Confidential (CSDF-LY) 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 this form will eventually become available to 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-LY form in order to not handicap their research efforts should they desire to follow up on your PIMS results.

FOR ALL CUSTOMERS SENDING THEIR OWN ANTIBODIES

E. Client-Supplied Antibody Description Forms (NSDF-AB and CSDF-AB)

For submitted antibodies, please ensure the following:

- Each antibody sample tube is labeled and properly identified on the form in Section B, including final concentration and volume
- In Section A, the customer must enter the unique Client Screen Identification Name from Box A of the Service Identification Form (PIMS-SIF) to match the antibody to the lysate to be used for immunoprecipitation with this antibody.
- The form is certified correct and signed and dated

F. Airway bill for Federal Express or any courier that accepts dry ice shipments

Complete the 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 or 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 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)

FOR U.S AND INTERNATIONAL CUSTOMER ONLY

G. 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.



Form: PIMS-SOF

PROTEIN IDENTIFICATION BY MASS SPECTROMETRY

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 Facsimile Number.

STUDY REPORTS

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

PRICING INFORMATION

Services offered for identification of antibody cross-reactive proteins by immunoprecipitation and mass spectrometry.

PRICING - Refer to Section D of the Sample Identification Forms: All prices in U.S. Funds. THE PROTEIN IDENTIFICATION IS CARRIED OUT IN TWO STAGES: 1ST STAGE BY IMMUNOPRECIPITATION OR IMMUNOAFFINITY, 2ND STAGE BY MASS SPECTROMETRY. Includes pricing table for antibodies and MS analysis, subtotal, and total cost for this order.

PAYMENT METHOD

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

Form fields for payment method: Print Cardholder Name, Visa Number, Expires (M/Y), 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:

Form fields for authorization: Print Name of Authorized Representative or Principal Investigator, Authorized Signature, Date (Y/M/D)

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



KINEXUS

Form: PIMS-SIF

PROTEIN IDENTIFICATION BY MASS SPECTROMETRY SERVICE IDENTIFICATION FORM

Subject to terms of the Kinexus Service Agreement

KINEXUS ORDER NUMBER

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

PROTEIN IDENTIFICATION BY MASS SPECTROMETRY SERVICE REQUESTED: (WITH CLIENT LYSATES)

Clients have the option of choosing antibodies provided by Kinexus or their own antibodies, or any combination thereof. Please refer to visit the Kinexus website at http://www.kinexus.ca/ourServices/massspec/proteinid.html to access the complete list of current antibodies available from Kinexus.

Form containing sections: SERVICE REQUESTED: PROTEIN IDENTIFICATION BY MS, KINEXUS ID NUMBER, A. CLIENT SCREEN ID NAME, B. ANTIBODY SELECTION, C. SAMPLE IDENTIFICATION, D. PRICING. Includes checkboxes for 'Client supplied' and 'New order', and pricing tables for IP and Mass Spectrometry Analysis stages.

Name of person completing this form _____ Signature _____ Date (Y/M/D) _____



KINEXUS

Form: NSDF-LY

FOR LYSATES 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)

Non-Confidential Service Requested and Lysate 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 lysates to Kinexus for testing. Clients are required to complete all Sections A-K to qualify for the Non-Confidential pricing level for the Kinexus' Proteomics Services if they provide their own lysates for analysis.

Form sections A through K containing various checkboxes and text input fields for client information, sample identification, species, tissues, cell states, fractionation, perturbations, and treatments.

I hereby certify that all the sample information provided in this order is correct and accurate to the best of my knowledge. To qualify for the non-confidential pricing level, I agree that all Sections A-K must be completed in full otherwise the confidential pricing level will be applied.

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



KINEXUS

Form: CSDF-LY

FOR LYSATES

CLIENT SUPPLIED CONFIDENTIAL SAMPLE DESCRIPTION FORM

Subject to terms of the Kinexus Service Agreement

KINEXUS ORDER NUMBER

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

Confidential Service Requested and Lysate 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 lysates to Kinexus for testing. Clients are required to complete Sections A-C for the Confidential pricing level for Kinexus' Proteomics Services if they provide their own lysates for analysis. Note that a Confidential analysis is performed at a higher pricing level than a Non-Confidential analysis. Clients should instead complete all of Sections A-C on the "Client-Supplied Non-Confidential Sample Description Form" (NSDF-LY) to qualify for the non-confidential pricing. To obtain 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 section 1: A. CLIENT SCREEN ID NAME + KINEXUS SERVICES NAME: CLIENT ID: _____ KINEXUS PROTEOMICS SERVICES NAME: _____ Use the Client ID Name that you entered in Box B on the Service Identification Form (SIF). The Kinexus Proteomics Services abbreviated name should be used from the SIF. B. SAMPLE IDENTIFICATION: Client Name for Sample: _____ Control: [] Yes [] No Concentration (mg/ml): _____ Volume (µl): _____ C. SPECIES: [] Human (Homo sapiens) Sex: [] Male [] Female [] M/F pooled [] Unknown [] Rat (Rattus norvegicus) # Animals: _____ Age: _____ Weight: _____ [] Mouse (Mus musculus) [] Other - Provide scientific & common name: _____ KINEXUS ID NUMBER (FOR INTERNAL USE ONLY) (Bar Code Identification Number)

Form section 2: A. CLIENT SCREEN ID NAME + KINEXUS SERVICES NAME: CLIENT ID: _____ KINEXUS PROTEOMICS SERVICES NAME: _____ Use the Client ID Name that you entered in Box B on the Service Identification Form (SIF). The Kinexus Proteomics Services abbreviated name should be used from the SIF. B. SAMPLE IDENTIFICATION: Client Name for Sample: _____ Control: [] Yes [] No Concentration (mg/ml): _____ Volume (µl): _____ C. SPECIES: [] Human (Homo sapiens) Sex: [] Male [] Female [] M/F pooled [] Unknown [] Rat (Rattus norvegicus) # Animals: _____ Age: _____ Weight: _____ [] Mouse (Mus musculus) [] Other - Provide scientific & common name: _____ KINEXUS ID NUMBER (FOR INTERNAL USE ONLY) (Bar Code Identification Number)

Form section 3: A. CLIENT SCREEN ID NAME + KINEXUS SERVICES NAME: CLIENT ID: _____ KINEXUS PROTEOMICS SERVICES NAME: _____ Use the Client ID Name that you entered in Box B on the Service Identification Form (SIF). The Kinexus Proteomics Services abbreviated name should be used from the SIF. B. SAMPLE IDENTIFICATION: Client Name for Sample: _____ Control: [] Yes [] No Concentration (mg/ml): _____ Volume (µl): _____ C. SPECIES: [] Human (Homo sapiens) Sex: [] Male [] Female [] M/F pooled [] Unknown [] Rat (Rattus norvegicus) # Animals: _____ Age: _____ Weight: _____ [] Mouse (Mus musculus) [] Other - Provide scientific & common name: _____ KINEXUS ID NUMBER (FOR INTERNAL USE ONLY) (Bar Code Identification Number)

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-AB

FOR ANTIBODIES **NON-CONFIDENTIAL** CLIENT-SUPPLIED 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 Antibody 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 antibodies to Kinexus for testing. For Non-Confidential pricing you must fully describe the nature of the probing antibodies (including immunogen sequence, the animal species in which the antibody was produced as well as manufacturer's name and catalogue number if it is commercially sourced). Please note that in the event that clients do not wish to disclose the source or nature of the antibodies that they are providing, then Confidential Pricing must apply. Clients must still complete Sections A to C for Confidential analyses. Please check the appropriate tick boxes. 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.

Form section 1: A. CLIENT SCREEN ID NAME + KINEXUS SERVICES NAME; B. ANTIBODY IDENTIFICATION; C. SPECIES OF ANTIBODY ORIGIN AND TYPE; D. COMMERCIAL SOURCE OF ANTIBODY; E. IMMUNOGEN INFORMATION; F. AMINO ACID SEQUENCE OF IMMUNOGEN

Form section 2: A. CLIENT SCREEN ID NAME; B. ANTIBODY IDENTIFICATION; C. SPECIES OF ANTIBODY ORIGIN AND TYPE; D. COMMERCIAL SOURCE OF ANTIBODY; E. IMMUNOGEN INFORMATION; F. AMINO ACID SEQUENCE OF IMMUNOGEN

I hereby certify that all of the information about antibodies that I provided in this order is correct and accurate to the best of my knowledge.

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



KINEXUS

Form: CSDF-AB

FOR ANTIBODIES

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 Antibody 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 antibodies to Kinexus for testing. For Confidential pricing you are not required to provide immunogen sequence, and manufacturer's name and catalogue number if it is commercially sourced. Clients must complete Sections A to C for Confidential analyses. Please check the appropriate tick boxes. 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.

Form section 1: A. CLIENT SCREEN ID NAME + KINEXUS SERVICES NAME; B. ANTIBODY IDENTIFICATION; C. SPECIES OF ANTIBODY ORIGIN AND TYPE; D. COMMERCIAL SOURCE OF ANTIBODY; E. IMMUNOGEN INFORMATION; F. AMINO ACID SEQUENCE OF IMMUNOGEN

Form section 2: A. CLIENT SCREEN ID NAME + KINEXUS SERVICES NAME; B. ANTIBODY IDENTIFICATION; C. SPECIES OF ANTIBODY ORIGIN AND TYPE; D. COMMERCIAL SOURCE OF ANTIBODY; E. IMMUNOGEN INFORMATION; F. AMINO ACID SEQUENCE OF IMMUNOGEN

I hereby certify that all of the information about antibodies that I provided in this order is correct and accurate to the best of my knowledge.

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

COMMERCIAL INVOICE

DATE OF EXPORTATION	EXPORT REFERENCES
SHIPPER/EXPORTER	CONSIGNEE 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
COUNTRY OF EXPORT	TERMS OF SALE Not for resale, sample for analysis
COUNTRY OF ORIGIN	PURPOSE Research and development
COUNTRY OF ULTIMATE DESTINATION Canada	EXPORTING CARRIER
INTERNATIONAL AIR WAYBILL NUMBER	
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 1.5 ml Eppendorf tubes:</i>	Non hazardous, non infectious protein for research and 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).	\$1.00 <i>per sample</i>
TOTAL NO. OF PACKAGES		TOTAL WEIGHT OF PACKAGES		TOTAL DECLARED VALUE
				\$

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)



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: _____

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). 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: _____