CPAP SERVICES

Version 13MY15

CUSTOM SERVICES

PEPTIDE ARRAY PRODUCTION
CUSTOMER INFORMATION PACKAGE

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TABLE OF CONTENTS

Custom Peptide Array Production (CPAP) Services

Service Ordering Information

Follow Up Services

Appendices - Forms to Complete and Return with Your Order

Custom Peptide Array Production (CPAP) Services

1. INTRODUCTION

As an important component of our unique integrated suite of proteomics services, Kinexus offers custom peptide array synthesis to assist our clients in their discovery programs. Peptide arrays are powerful tools for the investigation of protein-protein and drug-protein interactions. Screening peptides for potentially active compounds with peptide arrays is a very convenient method for basic and applied research such as drug development. In the following pages, we describe some of the principals and applications of peptide microarrays. A range of diverse peptide array-based services are available from Kinexus, and this package contains all of the information and forms required for our clients to utilize these services. For convenience, the various forms are available in fillable MS-Word versions that can be downloaded directly from the Kinexus website at http://www.kinexus.ca/ourServices/proteinAndPeptide/index.html or requested by e-mail from peptides@kinexus.ca.

For peptide-based drug design, with peptide microarrays it is possible to screen a high number of peptides on a small chip. However, due to the miniscule amounts of peptides synthesized directly on chips, and because of interactions of the peptides with the chip surface, this approach has proven to be difficult and often unreliable. These disadvantages can be overcome using peptide macroarrays on cellulose membranes. These are useful for solid-phase screening as well as solution-phase assays. Cellulose membranes are porous, hydrophilic, flexible and stable in organic as well as aqueous solvents. These properties make cellulose paper very useful for biochemical and biological studies in aqueous as well as in organic media and are a major reason why cellulose is still the most widely used material for macroarray membranes. Several hundred papers about applications using this method have been published (some of these are provided in Section 6). The spot densities of arrays range from a few up to approximately 8000 peptides.

Common cellulose membranes are not stable against harsh chemical conditions. Stable cellulose membranes are commercially available. Another development is the use of trifluoroacetic acid-soluble cellulose membranes. Peptides synthesized as macroarray on those membranes can be dissolved as peptide-cellulose conjugates and transferred in a large number of copies onto microarray glass slides keeping a three-dimensional structure with the high accessibility of cellulose-bound peptides (CelluSpots™).

The cellulose paper is usually functionalized with amino components like amino acids or amines. The attachment to cellulose is carried out either via ester or ether bonds. The ether bond is stable under common probing conditions, whereas the ester bond is labile and some loss can be

expected during the probing. This is why ester-type are more useful for generating peptides cleaved from the membrane in order to use them in solution assays.

The synthesis of the peptides is carried out chemically, starting with the C-terminal amino acid. The monitoring the coupling process takes place by staining the spots with bromophenol blue after selected coupling cycles. The very large number of different peptide sequences that could be synthesized on a macroarray means that coupling rates and amount, as well as purity of the peptides may vary. The synthesis quality of peptides using this technique is comparable to other solid-phase peptides synthesis methods until a length of 15 amino acids. The synthesis of longer peptides can lead to significant lower quality and quantity.

In contrast to biological systems, the chemical synthesis of peptides facilitates the introduction of non-natural amino acids and other organic building blocks. Also the selected use of modified amino acids (e.g phosphoamino acids) is possible. Additionally, post-synthesis modifications like acetylation, cyclizations of fluorescence labeling can be performed.

After the final synthesis step the peptides are displayed as free peptides bound to the cellulose with their C-terminus. Depending on the screening purpose, there are different format of peptide sets (e.g. epitope mapping, substitution analysis etc.) The probing of such peptide macroarrays can be performed similar to other dot-blot techniques.

2. MEMBRANES

We offer membranes with ester-type modifications as well as membranes with the ether-type.

The ester-type membranes are usually modified with an amino acid. Our standard modification is either with beta-alanine or glycine. But we also can use other modifications on demand. This type of membranes is very useful for the production of free peptides adsorbed by the membrane in order to use them in solution assays. For that purpose we would synthesize peptides in large dots big enough to get punched out using a common hole puncher. After cleavage from the cellulose, the peptides at the C-terminus will retain the amino acid from the membrane modification. The peptides can be easily dissolved in appropriate solvent. The amount of each peptide is between 200 and 300 nmol for a standard modification.

We offer two types of ether-type modified membranes: N-CAPE and TOTD membranes. N-CAPE (N-modified cellulose aminopropyl ether) membranes have a short aminopropyl molecule between the cellulose and the peptide. TOTD (trioxatridecanediamine) membranes display three

polyethylene-glycol units (PEG-3) between the cellulose and the peptides, which makes it more hydrophilic. This should result in less unspecific signals and background caused by hydrophobic interactions. The peptides are stable attached to either membranes and no loss on binding activity is expected.

Additionally we offer the use of chemically stable membranes, which we purchase from German suppliers. Those membrane are stable also against harsh chemical treatments, i.e. during strong regeneration procedures.

3. ARRAY FORMATS

Depending on the purpose of the screening, different array formats can be generated. The standard size of the spots containing peptides is between 1 and 2 mm in diameter (small spots). For solution arrays, we synthesize the peptides in spot with a diameter of 5-7 mm (large spots). In this section, we present some array techniques to screen for active peptides.

3.1. Epitope Mapping (Peptide Scan) - CPAP1

Epitope mapping is a very useful method for screening a known protein sequence for biologically active regions (e.g. epitopes for antibody binding). The peptide sequences are generated by shifting a frame with a distinct peptide length over a protein sequence of interest. A peptide length between 10 and 15 amino acids is commonly used. Shifting of the frame between 1 and 3 amino acids is recommended; the smaller the shift the more precise will be localization of the binding region.

3.2. Substitution Analysis (Replacement Analysis, Mutational Analysis) - CPAP2

Substitution analyses are used for investigation of the importance of amino acids and their possible exchanges in a known peptide sequence. The sequence of peptides in this array will be generated by successive systematic substitution of each amino acid by other amino acids or building blocks of interest. Our standard substitution analysis will be performed by the systematic exchange of all positions in the known peptide sequence by all 20 common amino acids. On demand, we would also perform substitution analyses by using non-natural amino acids or other organic building blocks. Number of peptides on the array are dependent on the starting length of the parent (wild-type) peptide, and the number of amino acids/building blocks used for the substitution.

3.3. Truncation Analysis (Length scan) - CPAP3

To investigate the minimum possible length of an active peptide while maintaining activity, variations of the peptide sequence are synthesized by systematic shortening by one amino acid residue at each step from the C-terminus, N-terminus, and both termini simultaneously. Number of peptides on the array are dependent on the starting length of the parent (wild-type) peptide.

3.4. Random Peptide Library - CPAP4

To screen for active peptides without prior knowledge of a starting sequence, a random peptide library can be used. This array contains randomized peptide sequences. Compared with the combinatorial peptide library, the advantage of the random peptide array is that the peptides on each spot are unique, providing the possibility of higher individual activity. The disadvantage is in the relative low number of synthesized peptides available for screening. Our standard random peptide library contains 1200 peptide sequences with a length of 12 or 15 amino acids. But a synthesis of random peptide libraries based on other parameters is feasible.

3.5. Combinatorial Peptide Library - CPAP5

A very powerful method for screening active peptides without knowing the actual sequence is the combinatorial peptide library. Using combinatorial libraries, screening begins in theory with the entire pool of possible peptide sequences. Due to the impossibility of synthesizing all peptides as single sequences (for instance all possible 6-mers of the common 20 L-amino acids would result in 64,000,000 peptide sequences), in the first screening rounds a mixture of all possible amino acids and building blocks of interest would be used at most positions. To achieve distinct single sequences, a deconvolution over several synthesis and screening rounds is necessary. In practice, for the first round of synthesis and screening all but two positions include mixtures of amino acids or building blocks of interest. Following that, each peptide consists of a sequence with several mixed positions and two defined amino acids. The number of synthesized sequences is a combination of the number of used amino acid in these two defined positions. For instance, if at these two positions the common 20 L-amino acids were used, one would obtain 20x20=400 sequences. For a better overview the spots in an array would be arranged in a chessboard pattern with 20 rows and 20 columns. In each single row would represent all amino acids used at one position and combined it with the column-wise display for the other position. By screening one would obtain signals on spots with active sequence patterns. After the first synthesis and screening round there are two possibilities: First, one can combine different sequence patterns to a complete sequence. The second possibility is to select the sequence pattern with the strongest activity, keep the amino acid motif for these two positions, and perform a new synthesis and

screening round for deconvolution of other two mixture positions. This repeating of deconvolution, synthesis and screening cycles proceeds until one obtains a complete sequence in which all amino acid positions are defined. The standard size of peptides in a combinatorial library is 6- to 8-mers, which would need 3 or 4 synthesis and screening rounds to achieve defined peptide sequences. The number of spots depends on the number of amino acids used for the combinations.

3.6. Cluster Peptide Library - CPAP6

To reduce the number of possibilities, combine several amino acids of similar properties in clusters (e.g. hydrophobicity – Ile, Leu, Val; or steric similarity – Ser, Cys, Abu). These clusterered amino acid peptide libraries provide easier and faster screening of large peptide libraries. It is a very useful alternative screening method to combinatorial and random peptide libraries. It is of course necessary to resolve these clusters at the end of the screening process.

3.7. Loop Scan (Cysteine Scan) - CPAP7

To stabilize loop structures or to increase their resistance to proteolytic digestion, it is convenient to cyclize peptides. There are two main types of cyclizations – cyclization via cysteines forming a disulfide bridge and cyclization via a pair of peptide amino and carboxy groups to form an amide bond. In both cases, a pair of amino acids are involved. If they are not present in the original peptide sequence, they must be inserted or two existing amino acids should be replaced which could lead to a loss of activity. Therefore, it is necessary to investigate the effect of the insertion/exchange and cyclization on the activity of the peptide. Our standard loop scan is a cysteine loop scan that contains a set of all possible combinations of insertions or replacements using a pair of cysteines. If requested, we could also perform an amide loop scan. Number of peptides on the array are dependent on the starting length of the parent (wild-type) peptide.

3.8. Customized Peptide Library - CPAP8

Our CPAP8 service offers also to synthesize a peptide macroarray on cellulose with a set of peptide sequences developed by our customers.

4. SOLUBLE PEPTIDES ON CELLULOSE

We also offer soluble peptides absorbed on the cellulose produced from each of the CPAP1 to CPAP8 services, but each peptide must be generated in large spots. The released peptides can be punched out and dissolved in an appropriate solvent and can be used for solution assays. Due to the modification of the membrane, these peptides are usually delivered as peptide amides with an additional amino acid C-terminal attached to the sequence. Standard amino acids for this

additional amino acid are beta-Ala or Gly. The peptides attached to the cellulose can be delivered as a sheet or as a set of small paper discs.

5. CELLUSPOTS™ MICROARRAYS – CPAPA AND CPAPB

We are pleased to offer our customers the possibility of using CelluSpots™ microarrays. This microarray consist of peptide-cellulose conjugates on each spot. It combines the advantages of a common microarray on glass slides with the high accessibility and three-dimensional structure of cellulose-bound peptides. The three-dimensional structure contains up to 100 times more peptide per area than conventional monolayer deposition.

Up to 384 spots could be printed in duplicates. An order for this type of arrays is useful, if many copies of arrays with many peptides are needed. Additionally, we offer ready-to-screen kinase-substrate peptide microarrys from annotated phosphorylation sites produced with the CelluSpots™ method.

6. REFERENCES

Synthesis of Peptide Macroarrays using SPOT Technique

- Ay, B., Volkmer, R.& Boisguerin, P. (2007) Synthesis of cleavable peptides with authentic C-termini: An application for fully automated SPOT synthesis. *THL* **48**:361–364.
- Frank, R. (1992) Spot-synthesis: An easy technique for the positionally addressable, parallel chemical synthesis on a membrane support. *Tetrahedron* **48**:9217—9232
- Hilpert, K., Winkler, D.F.H. & Hancock, R.E.W. (2007) Peptide arrays on cellulose support: SPOT synthesis - a time and cost efficient method for synthesis of large numbers of peptides in a parallel and addressable fashion. *Nature Protocols* **2**(6):1333-1349
- Hoffmann, B., Ast, T., Polakowski, T., Reineke, U. & Volkmer, R. (2006) Transformation of a biologically active peptide into peptoid analogs while retaining biological activity. *Prot. Pept. Lett.* **13**:829-833
- Koch, J. & Mahler, M. (Eds.), *Peptide Arrays on Membrane Support*. Springer-Verlag, Berlin Heidelberg, Germany
- Kramer, A. & Schneider-Mergener, J. (1998) Synthesis and application of peptide libraries bound to continuous cellulose membranes. *Meth. Mol. Biol.* **87**:25-39
- Kramer, A., Reineke, U., Dong, L. et al. (1999) Spot-synthesis: observations and optimizations. *J. Pept. Res.* **54**:319-327
- Molina, F., Laune, D., Gougat, C., Pau, B. & Granier, C. (1996) Improved performances of spot multiple peptide synthesis. *Pept. Res.* **9**:151-155
- Schneider-Mergener, J., Kramer, A. & Reineke, U. (1996) Peptide libraries bound to continuous cellulose membranes: Tools to study molecular recognition. In: *Combinatorial Libraries: Synthesis, Screening and Application Potential*, ed. R. Cortese, New York: Walter de Gruyter
- Tapia, V., Ay, B., Triebus, J., Wolter, E., Boisguerin, P. & Volkmer, R. (2008) Evaluating the coupling efficiency of phosphorylated amino acids for SPOT synthesis. *J. Pept. Sci.* **14**:1309–1314
- Volkmer, R. (2009) Synthesis and Application of Peptide Arrays: Quo Vadis SPOT Technology. *ChemBioChem* **10**:1431-1442

- Winkler, D.F.H.& Campbell, William D. (2008) The Spot Technique: Synthesis and Screening of Peptide Macroarrays on Cellulose Membranes. *Meth. Mol. Biol.* **494**:47-70
- Winkler, D.F.H. & McGeer, P.L. (2008) Protein labeling and biotinylation of peptides during spot synthesis using biotin p-nitrophenyl ester (biotin-ONp). *Proteomics* **8**:961–967

Applications of Peptide Macroarrays Synthesized by SPOT Method

- Akita, S., Umezawa, N., Kato, N. & Higuchi, T. (2008) Array-based fluorescence assay for serine/threonine kinases using specific chemical reaction. *Bioorg. Med. Chem.* **16**:7788–7794
- Bhargava, S., Licha, K., Knaute, T. et al. (2002) A complete substitutional analysis of VIP for better tumor imaging properties. *J. Mol. Recognit.***15**:145-153
- Bialek, K., Swistowski, A. & Frank, R. (2003) Epitope-targeted proteome analysis: towards a large-scale automated protein-protein-interaction mapping utilizing synthetic peptide arrays. *Anal. Bioanal. Chem.* **376**:1006-1013
- Boisguerin, P., Leben, R., Ay, B. et al. (2004) An improved method for the synthesis of cellulose membrane-bound peptides with free C termini is useful for the PDZ domain binding studies. *Chem. Biol.* **11**:449-459
- Bolger, G.B., Baillie, G.S., Li, X. et al. (2006) Scanning peptide array analyses identify overlapping binding sites for the signaling scaffold proteins, □-arrestin and RACK1 in the cAMP-specific phosphodiesterase, PDE4D5. *Biochem. J.* **398**:23-36
- Buss, H., Dörrie, A., Schmitz, M.L. et al. (2004) Phosphorylation of serine 468 by GSK-3□ negatively regulates basal p65 NF-□B activity. *J. Biol. Chem.* **279**:49571-49574
- Espaniel, X. & Sudol, M. (2001) Yes-associated protein and p53-binding protein-2 interact through their WW and SH3 domains. *J. Biol. Chem.* **276**:14514-14523
- Frank, R. (2002) The SPOT-synthesis technique. Synthetic peptide arrays on membrane supports-principles and applications. *J. Immun. Meth.* **267**:13-26
- Frank, R. & Overwin, H. (1996) SPOT synthesis. Epitope analysis with arrays of synthetic peptides prepared on cellulose membranes. In: *Meth. Mol. Biol.*, vol. **66**: *Epitope mapping protocols*, ed. G.E. Morris, pp.149-169. Totowa, NJ: Humana Press
- Frese, S., Schubert, W.-D., Findeis, A.C. et al. (2006) The phosphotyrosine peptide binding specificity of Nck1 and Nck2 SH2 domains. *J. Biol. Chem.* **281**:18236-18245
- Grogan, J.L., Kramer, A., Nogai, A. et al. (1999) Cross-reactivity of myelin basic protein-specific T cells with multiple microbial peptides: Experimental autoimmune encephalomyelitis induction in TCR transgenic mice. *J. Immunol.* **163**:3764-3770
- Hahn, M., Winkler, D., Welfle, K. et al. (2001) Cross-reactive binding of cyclic peptides to an anti-TGF□ antibody Fab fragment. An X-ray structural and thermodynamic analysis. *J. Mol. Biol.* **314**:293-309
- Hilpert, K., Elliott, M., Jenssen, H. et al. (2009) Screening and characterization of surface-tethered cationic peptides for antimicrobial activity. *Chem. Biol.* **16**:58–69
- Hilpert, K., Elliott, M.R., Volkmer-Engert, R. at al. (2006) Sequence requirements and an optimization strategy for short antimicrobial peptides. *Chem. Biol.* **13**:1101-1107
- Hilpert, K., Winkler, D.F.H. & Hancock, R.E.W. (2007) Cellulose-bound peptide arrays: Preparation and applications. *Biotechnol. Genet. Engin. Rev.* **24**:31-106
- Kamradt, T. & Volkmer-Engert, R. (2004) Cross-reactivity of T lymphocyctes in infection and autoimmunity. *Mol. Divers.* **8**:271-280
- Koch, J. & Mahler, M. (Eds.), *Peptide Arrays on Membrane Support*. Springer-Verlag, Berlin Heidelberg, Germany
- Kramer, A., Keitel, T., Winkler, K. et al. (1997) Molecular basis for the binding promiscuity of an anti-p24 (HIV-1) monochlonal antibody. *Cell* **91**:799-809

- Kramer, A., Stigler, R.-D., Knaute, T., Hoffmann, B. & Schneider-Mergener, J. (1998) Stepwise transformation of a cholera toxin an a p24 (HIV-1) epitope into D-peptide analogs. *Prot. Engin.* **11**:941-948
- Kramer, A., Vakalopoulou, E., Schleuning, W.-D. & Schneider-Mergener, J. (1995) A general route to fingerprint analyses of peptide-antibody interactions using a clustered amino acid peptide library: Comparison with a phage display library. *Mol. Immunol.* **32**:459-465
- Liang, M., Mahler, M., Koch, J. et al. (2003) Generation of an HFRS patient-derived neutralizing recombinant antibody to Hantaan virus G1 protein and definition of the neutralizing domain. *J. Med. Virol.* **69**:99-107
- Mahler, M., Kessenbrock, K., Raats, J. et al. (2003) Characterization of the human autoimmune response to the major C-terminal epitope of the ribosomal P proteins. *J. Mol. Med.* **81**:194-204
- Malin, R., Steinbrecher, R., Jannsen, J. et al. (1995) Identification of Technetium-99m binding peptides using combinatorial cellulose-bound peptide libraries. *JACS* **117**:11821-11822
- Martens, W., Greiser-Wilke, I., Harder, T.C. et al. (1995) Spot synthesis of overlapping peptides on paper membrane supports enables the identification of linear monoclonal antibody binding determinants on morbillivirus phosphoproteins. *Vet. Microbiol.* **44**:289-298
- Münch, G., Schicktanz, D., Behme, A. et al. (1999) Amino acid specificity of glycation and protein-AGE crosslinking reactivities determined with a dipeptide SPOT library. *Nature Biotechnol.* **17**:1006-1010
- Oggero, M., Frank, R., Etcheverrigaray, M. & Kratje, R. (2004) Defining the antigenic structure of human GM-CSF and its implications for the receptor interaction and therapeutic treatments. *Mol. Divers.* **8**:257-269
- Otvos Jr., L., Pease, A.M., Bokonyi, K. et al. (2000) In situ stimulation of a T helper cell hybrodoma with a cellulose-bound peptide antigen. *J. Immunol. Meth.s* **233**:95-1051
- Piossek, C., Thierauch, K.-H., Schneider-Mergener, J. et al. (2003) Potent inhibition of angiogenesis by D, L-peptides derived from vascular endothelial growth factor receptor 2. *Thromb. Haemost.* **90**:501-510
- Przezdziak, J., Tremmel, S., Kretzschmar, I. et al. (2006) Probing the ligand-binding specificity and analyzing the folding state of SPOT-synthesized FBP28 WW domain variants. *ChemBioChem* **7**:780-788
- Pulli, T., Lankinen, H., Roivainen, M. & Hyypiä, T. (1998) Antigenic sites of coxsackievirus A9. *Virology* **240**:202-212
- Reineke, U., Ivascu, C., Schlief, M. et al. (2002) Identification of distinct antibody epitopes and mimotopes from a peptide array of 5520 randomly generated sequences. *J. Immunol. Meth.* **267**:37-51
- Reineke, U., Kramer, A. & Schneider-Mergener, J. (1999b) Antigen sequence- and library-based mapping of linear and discontinuous protein-protein-interaction sites. In: *Current Topics in Microbiology and Immunology* **243**:23-36, eds. M. Famuluk et al., Berlin Heidelberg: Springer-Verlag
- Reineke, U., Sabat, R., Volk, H.-D. & Schneider-Mergener, J. (1998) Mapping of the interleukin-10/interleukin-10 receptor combining site. *Prot. Sci.* **7**:951-960
- Reineke, U., Sabat, R., Kramer, A. et al. (1996) Mapping protein-protein contact sites using cellulose-bound peptide scans. *Mol. Divers.* **1**:141-148
- Reineke, U., Volkmer-Engert, R., & Schneider-Mergener, J. (2001) Applications of peptide arrays prepared by the SPOT-tecnology. *Curr. Opinion Biotechnol.* **12**:59-64
- Santona, A., Carta, F., Fraghi, P. & Turrini, F. (2002) Mapping antigenic sites of an immunodominant surface lipoprotein of Mycoplasma agalactiae, AvgC, with the use of synthetic peptides. *Infect. Immun.* **70**:171-176

- Schutkowski, M., Reineke, U. & Reimer, U. (2005) Peptide arrays for kinase profiling. *ChemBioChem* **6**:513-521
- Tegge, W., Frank, R., Hofmann, F. & Dostmann, R.G. (1995) Determination of cyclic nucleotide-dependent protein kinase substrate specificity by the use of peptide libraries on cellulose paper. *Biochemistry* **34**:10569-10577
- Toepert, F., Pires, J.R., Landgraf, C., Oschkinat, H. & Schneider-Mergener, J. (2001) Synthesis of an array comprising 837 variants of the hYAP WW protein domain. *Angew. Chemie Int. Ed.* **40**:897-900
- Welschof, M., Reineke, U., Kleist, C. et al. (1999) The antigen binding domain of non-idiotypic human anti-$F(ab')_2$ autoantibodies: Study of their interaction with IgG hinge region epitopes. *Human Immunol.* **60**:282-290

Peptide Microarrays

- Andresen, H., Grötzinger, C., Zarse, K., Kreuzer, O.J., Ehrentreich-Förster, E. and Bier, F.F. (2006) Functional peptide microarrays for specific and sensitive antibody diagnostics. *Proteomics* **6**:1376-1384
- Beutling, U., Städing, K., Stradal, T. & Frank, R. (2008) Large-scale analysis of protein–protein interactions using cellulose-bound peptide arrays. *Adv. Biochem. Engin./Biotechnol*. **110**:115–152.
- Dikmans, A., Beutling, U., Schmeisser, E., Thiele, S. and Frank, R. (2006) SC^2: A novel process for manufacturing multipurpose high-density chemical microarrays. *QSAR & Comb. Sci.* **25**:1069-1080
- Maier, S., Frank, M., Rau, H., Lewandrowski, P., Uhrig, R., Keil, O., Deppe, H., Müller, N., Vanier, C., Mannsperger, H., Zepter, S. and Junker, H.-D. (2006) Synthesis and quality control of thiol compound libraries for chemical microarrays. *QSAR & Comb. Sci.* **25**:1047-1054.
- Reineke, U., Schneider-Mergener, J. and Schutkowski, M. (2006) Peptide arrays in proteomics and drug discovery. In: *BioMEMS and Biomedical Nanotechnology, Vol.II: Micro/Nano technologies for genomics and proteomics,* eds. M. Ferrari, M. Ozkan and M.I. Heller, pp. 911-916, Springer US, New York/Boston, USA
- Winkler, D.F.H., Andresen, H. & Hilpert, K. (2010) SPOT synthesis as a tool to study protein-protein interactions. *Meth. Mol. Biol.* (in press)
- Winkler, D.F.H., Hilpert, K.; Brandt, O.& Hancock, R.E.W. (2009) Synthesis of peptide arrays using SPOT-technology and CelluSpots-method. *Meth. Mol. Biol.* **570**:157-174

7. TURNAROUND TIME

The turnaround time for these services is estimated to be 3 to 4 weeks. However, this could varies slightly according to the size of the and the demand of the service at the time when the is placed. Each arrayed will be delivered with a comprehensive report.

8. PRICING INFORMATION

CPAP1-8 Custom Peptide Arrays on Cellulose Membranes

Kinexus Custom Peptide Array Production (CPAP) Services offers different types of macroarrays. The price depends on the number of peptides and their length. For the estimation of the price you

have to calculate the number of units (number of peptides x peptide length x number of copies). The following prices in U.S. dollars are per amino acid residue and peptide for small spots (for larger spots we will charge 50% more):

Up to units	Price per unit
625	0.48
754	0.47
889	0.46
1030	0.45
1178	0.44
1332	0.43
1493	0.42

Up to units	Price per unit
1663	0.41
1841	0.4
2028	0.39
2225	0.38
2432	0.37
2652	0.36
2883	0.35

Up to units	Price per unit
3128	0.34
3388	0.33
3665	0.32
3959	0.31
4273	0.3
4608	0.29
4968	0.28

Up to units	Price per unit
5354	0.27
5769	0.26
6218	0.25
6705	0.24
7233	0.23
7810	0.22
8442	0.21

Up to units	Price per unit
9136	0.2
9904	0.19
10758	0.18
11711	0.17
12784	0.16

More than 14,000 units would cost 0.15 USD per unit.

Prices for membranes:	beta-Ala	$ 20.00
	CAPE	$ 50.00
	TOTD	$ 50.00
	Commercial membrane	$ 200.00

Minimum order volume is $ 300.00 (without membrane).

Additionally charges will be applied to the membranes used for the array, a release of peptides from the membrane as well as peptide modifications. Contact Dr. Dirk Winkler at peptides@kinexus.ca for pricing.

CPAPA - CelluSpots™ Custom Peptide Arrays on Glass Slides

- Standard format 26x76 mm glass slides covered with white adhesive foil
- Up to 384 unique spots printed in duplicates
- 1.2 mm spot to spot distance
- Contains control peptides and location marks

# Peptides	Peptide Length	# Slides	Price [USD]
Max. 96	8-15	20	4000.00
Max. 192	8-15	20	5000.00
Max. 288	8-15	20	5800.00
Max. 384	8-15	20	6600.00
Extra slides	with initial order	set of 20	1200.00
Extra slides	with initial order	set of 40	1900.00
Extra slides	reprinted*	set of 20	1350.00
Extra slides	reprinted*	set of 40	2050.00

Note: Longer peptides 16-20 amino acids add 5% and for 21-25 amino acids add 10%.

CPAPB - CelluSpots™ Kinase Substrate Peptide Arrays on Glass Slides

Ready to screen arrays with protein-tyrosine and protein-serine/threonine kinase substrates from annotated phosphorylation sites. This is an ideal tool to characterize substrate specificities of kinases, to compare kinases, to identify potential autophosphorylation sites, or to screen for kinase inhibitors.

Array	Spots per Slide	Slides	Price [USD]
Protein-tyrosine Kinase Substrates	384 in duplicate	pack of 4	780.00
	384 in duplicate	> pack 5	650.00
Protein-serine/threonine Kinase Substrates I + II (2 arrays)	384 in duplicate	pack of 4 pairs (= 8 slides)	1080.00
	384 in duplicate	> pack of 5	850.00
Test Packs			
Protein-tyrosine Kinase I Plus (1 array)	384 in duplicate	2 duplicate	380.00
Protein-serine/threonine Kinase Substrates I + II (2 arrays)	384 in duplicate	1 pair	380.00

9. FORMS TO BE COMPLETED

All customers are required to complete the following forms for each order placed:

A. Kinexus Proteomics Services Agreement.
B. Service Order Form (CPAP-SOF). The Service Order Form (SOF) allows us to obtain client contact and billing information and establish the cost of the order.
C. Service Identification Form (CPAP-SIF). The Service Identification Form (SIF) permits us to determine which specific Custom Peptide Array Production Services are requested.

A. Kinexus Proteomics Services Agreement

- A signed Kinexus Proteomics Services Agreement is required before your first order with Kinexus 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 (CPAP-SOF)

Please ensure:

- Shipping address and contact name and numbers are specified.
- Billing information is completed.
- 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 Forms (CPAP_-SIF)

Note that:

- Fillable MS-Word versions of all of these CPAP-SIF forms and the CPAP-SOF are available for download from the Kinexus website at the bottom of the webpage http://www.kinexus.ca/ourServices/proteinAndPeptide/index.html. Such electronically completed forms can be sent via email for rapid processing of orders. For direct request of such fillable MS-Word forms as well as for all enquiries related to peptide synthesis and array technical/research issues, work orders, and service fees, please contact Dr. Dirk Winkler by email at peptides@kinexus.ca or by phone at 604-323-2547 Ext.17.

- The service identification forms (SIF) allows us to track all of the various services to be used within an order. For each of the different array types there is a separate order form:

i. CPAP1-SIF Form - Epitope Mapping
ii. CPAP2-SIF Form - Substitution Analysis
iii. CPAP3-SIF Form - Truncation Analysis
iv. CPAP4-SIF Form - Random Peptide Library
v. CPAP5-SIF Form - Combinatorial Library
vi. CPAP6-SIF Form - Cluster Peptide Library
vii. CPAP7-SIF Form - Loop Scan
viii. CPAP8-SIF Form - Customized Peptide Library
ix. CPAPA-SIF Form - CelluSpots Custom Peptide Array
x. CPAPB-SIF Form - CelluSpots Kinase Substrate Array

- For each CPAP service used, please assign a unique name (Client ID Name) to be entered on the Service Order Form (CPAP-SOF).

When Kinexus received the all information complete and correct, you will receive a confirmation of the specifics for your order, including pricing. We will not proceed with your order until we have received verification of your approval to go ahead and process your order.

10. FOLLOW UP SERVICES

Kinexus offers also a testing service for synthesized macroarrays on cellulose. We would perform this testing along with a negative control. The necessary protein/antibody is either provided by the customer or, if available, we would purchase it, with additional cost to the client. Unless there are other instructions from the customer, the treatment will be carried out similar to other blotting techniques. The bound protein would be detected via HRP/chemiluminescence, but staining would also be possible.

The price would be at US $ 500 per sample (excluding possible charge for purchase of protein). The probing would be carried out only if we receive payment of 50% of the total price in advance after the successful synthesis.

Please contact Dr. Dirk Winkler by email at peptides@kinexus.ca or by phone at 604-323-2547 Ext.17.

KINEXUS

Form: CPAP-SOF

CUSTOM PEPTIDE ARRAY PRODUCTION

SERVICE ORDER FORM

Subject to terms of the Kinexus Proteomics Services Agreement

KINEXUS ORDER NUMBER

CUSTOMER INFORMATION ☐ REPEAT CUSTOMER OR ☐ NEW CUSTOMER

☐ Dr. ☐ Mr. ☐ Ms.

Name of Authorized Representative or Principal Investigator | *Title/Position*

Company Name or Institute | *Department*

Street Address

City | *State or Province* | *Country* | *Zip or Postal Code*

Email Address | *(Area Code) Telephone Number* | *(Area Code) Facsimile Number*

Contact Person (if different from Authorized Representative) | *Email Address* | *(Area Code) Telephone Number*

CUSTOM PEPTIDE ARRAY PRODUCTION SERVICES

REQUESTED PRODUCTS SHIPPED TO: ☐ AUTHORIZED REPRESENTATIVE/INVESTIGATOR **OR** ☐ CONTACT PERSON

REQUESTED WORK AND PRICING INFORMATION *(For price per service, refer to CPAP Customer Information Package or quotation.)*

Description:	**CPAP-SIF ID Name(s)** *(From Box B of CPAP-SIF)*	**Cost (U.S. Currency)**
CPAP1 - Epitope Mapping (Peptide Scan)		$
CPAP2 - Substitution Analysis (Replacement, Mutation)		$
CPAP3 - Truncation Analysis (Length Scan)		$
CPAP4 - Random Peptide Library		$
CPAP5 - Combinatorial Peptide Library		$
CPAP6 - Cluster Peptide Library		$
CPAP7 - Loop Scan (Cysteine Scan)		$
CPAP8 - Customized Peptide Library		$
CPAPA - CelluSpots™ Custom Peptide Arrays		$
CPAPB - CelluSpots™ Kinase Substrate Peptide Arrays		$

Total number of CPAP services requested with this order:____ **SUBTOTAL** = $

Quotation or Reference Number: _____ - $

Shipping and handling + $

TOTAL COST FOR THIS ORDER = $

FOR CANADIAN CUSTOMERS ONLY:

Add an additional 5% to the above total for GST (No. 893907329 RT0001): + $ = $

TOTAL AMOUNT PAYABLE IN U.S FUNDS

PAYMENT METHOD

☐ PURCHASE ORDER ACCEPTED FROM COMPANIES AND INSTITUTES WITH APPROVED CREDIT. P.O. NUMBER: _____

☐ VISA OR ☐ MASTERCARD

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:

☐ Dr ☐ Mr ☐ Ms

Accounts Payable Contact Name | *Company Name or Institute*

Street Address | *City*

State or Province | *Country* | *Zip or Postal Code* | *(Area Code) Telephone Number*

AUTHORIZATION

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

Print Name of Authorized Representative or Principal Investigator | *Authorized Signature* | *Date y/m/d)*

How did you originally hear about the CPAP Services? ☐ ***Direct Mail*** ☐ ***Email*** ☐ ***Web Site*** ☐ ***Advertisement*** ☐ ***Referral*** ☐ ***Conference or Trade Show*** ☐ ***Other***

KINEXUS

Form: CPAP1-SIF

KINEXUS ORDER NUMBER
For Kinexus internal use only.

CUSTOM PEPTIDE ARRAY PRODUCTION

PRELIMINARY

SERVICE IDENTIFICATION FORM

Subject to terms of the Kinexus Proteomics Services Agreement

NAME: **COMPANY/INSTITUTE:**

(Authorized Representative or Principal Investigator)

Particulars of Service Requested:

Please refer to the CPAP Services Customer Information Package for further details about these services. Complete the sections and check the boxes as appropriate. Blue areas are for Kinexus use only and should not be filled. An electronic fillable copy of this form is available from Kinexus. If you need assistance completing this form, contact Dr. Dirk Winkler by calling toll free in North America 1-866-KINEXUS (866-546-3987) or by email at peptides@kinexus.ca.

A. CUSTOM SERVICE REQUESTED:

☐ **Epitope Mapping (Peptide Scan) (CPAP1)**

Peptide screening of a known sequence on a cellulose membrane.

KINEXUS ID NUMBER
(Bar Code Identification Number)
For Kinexus internal use only.

B. CPAP1-SIF IDENTIFICATION NAME:

Client ID:

Use this ID name of your choice for your internal reference and completion of the CPAP-SOF form.

C. DESCRIPTION: Protein Amino Acid Sequence (Wild-type)

For proteins with more than 400 amino acids, please provide the full sequence as an attachment.

File name for attachment with peptide sequence: _____

				Protein Name (Not required)	Product Code Kinexus use only.	Cost U.S. $ Kinexus use only.
1.	1	01 02 03 04 05 06 07 08 09 10 11 12 13 14 15 16 17 18 19 20 21 22 23 24 25 26 27 28 29 30 31 32 33 34 35 36 37 38 39 40	40			
2.	41	01 02 03 04 05 06 07 08 09 10 11 12 13 14 15 16 17 18 19 20 21 22 23 24 25 26 27 28 29 30 31 32 33 34 35 36 37 38 39 40	80			
3.	81	01 02 03 04 05 06 07 08 09 10 11 12 13 14 15 16 17 18 19 20 21 22 23 24 25 26 27 28 29 30 31 32 33 34 35 36 37 38 39 40	120			
4.	121	01 02 03 04 05 06 07 08 09 10 11 12 13 14 15 16 17 18 19 20 21 22 23 24 25 26 27 28 29 30 31 32 33 34 35 36 37 38 39 40	160			
5.	161	01 02 03 04 05 06 07 08 09 10 11 12 13 14 15 16 17 18 19 20 21 22 23 24 25 26 27 28 29 30 31 32 33 34 35 36 37 38 39 40	200			
6.	201	01 02 03 04 05 06 07 08 09 10 11 12 13 14 15 16 17 18 19 20 21 22 23 24 25 26 27 28 29 30 31 32 33 34 35 36 37 38 39 40	240			
7.	241	01 02 03 04 05 06 07 08 09 10 11 12 13 14 15 16 17 18 19 20 21 22 23 24 25 26 27 28 29 30 31 32 33 34 35 36 37 38 39 40	280			
8.	281	01 02 03 04 05 06 07 08 09 10 11 12 13 14 15 16 17 18 19 20 21 22 23 24 25 26 27 28 29 30 31 32 33 34 35 36 37 38 39 40	320			
9.	321	01 02 03 04 05 06 07 08 09 10 11 12 13 14 15 16 17 18 19 20 21 22 23 24 25 26 27 28 29 30 31 32 33 34 35 36 37 38 39 40	360			
10.	361	01 02 03 04 05 06 07 08 09 10 11 12 13 14 15 16 17 18 19 20 21 22 23 24 25 26 27 28 29 30 31 32 33 34 35 36 37 38 39 40	400			

D. SPOT SPECIFICATION:

☐ Small ☐ Large
☐ Uncleaved ☐ Cleaved

E. MEMBRANE TYPE:

☐ Commercial ☐ CAPE
☐ Beta-Ala ☐ TOTD
☐ Others: _____

F. NUMBER OF COPIES:
State the number of copies of the array.

_____

G. PEPTIDE TYPE:

☐ Linear
☐ C-C-cyclic
☐ Amide cyclic

H. PEPTIDE INFORMATION:

Length of primary sequence: _____ aa

Length of desired peptides: _____ aa

Shift sequence by _____ aa

Number of peptides: _____ (Kinexus only)

I. N-TERMINUS:

☐ Free amino group
☐ Acetylated
☐ Other modification:

_____

J. PROBING INCUBATION:

1st incubation (Sample): _____

_____

2nd incubation (Detection: _____

_____

Detection method: _____

K. CONTROL INCUBATION:

1st incubation (Sample): _____

_____

2nd incubation (Detection: _____

_____

Detection method: _____

I. REMARKS:

_____

Name of person completing this form *Email Address/Facsimile Number/ Phone Number* *Date (y/m/d)*

KINEXUS

Form: CPAP2-SIF

KINEXUS ORDER NUMBER
For Kinexus internal use only.

CUSTOM PEPTIDE ARRAY PRODUCTION

PRELIMINARY

SERVICE IDENTIFICATION FORM

Subject to terms of the Kinexus Proteomics Services Agreement

NAME: **COMPANY/INSTITUTE:**

(Authorized Representative or Principal Investigator)

Particulars of Service Requested:

Please refer to the CPAP Services Customer Information Package for further details about these services. Complete the sections and check the boxes as appropriate. Blue areas are for Kinexus use only and should not be filled. An electronic fillable copy of this form is available from Kinexus. If you need assistance completing this form, contact Dr. Dirk Winkler by calling toll free in North America 1-866-KINEXUS (866-546-3987) or by email at peptides@kinexus.ca.

A. CUSTOM SERVICE REQUESTED:

☐ **Replacement (Substitution) Analysis (CPAP2)**

Systematic exchange of amino acids of a given peptide sequence (wild-type).

KINEXUS ID NUMBER
(Bar Code Identification Number)
For Kinexus internal use only.

B. CPAP2-SIF IDENTIFICATION NAME:

Client ID: _____

Use this ID name of your choice for your internal reference and completion of the CPAP-SOF form.

C.	DESCRIPTION: Amino Acid Sequence (Wild-type)	Protein Name (Not required)	Product Code Kinexus use only.	Cost U.S. $ Kinexus use only.
1.	N-T 01 02 03 04 05 06 07 08 09 10 11 12 13 14 15 16 17 18 19 20 21 22 23 24 25 26 27 28 29 30 31 32 33 34 35 36 37 38 39 40 C-T			
2.	N-T 01 02 03 04 05 06 07 08 09 10 11 12 13 14 15 16 17 18 19 20 21 22 23 24 25 26 27 28 29 30 31 32 33 34 35 36 37 38 39 40 C-T			
3.	N-T 01 02 03 04 05 06 07 08 09 10 11 12 13 14 15 16 17 18 19 20 21 22 23 24 25 26 27 28 29 30 31 32 33 34 35 36 37 38 39 40 C-T			
4.	N-T 01 02 03 04 05 06 07 08 09 10 11 12 13 14 15 16 17 18 19 20 21 22 23 24 25 26 27 28 29 30 31 32 33 34 35 36 37 38 39 40 C-T			
5.	N-T 01 02 03 04 05 06 07 08 09 10 11 12 13 14 15 16 17 18 19 20 21 22 23 24 25 26 27 28 29 30 31 32 33 34 35 36 37 38 39 40 C-T			
6.	N-T 01 02 03 04 05 06 07 08 09 10 11 12 13 14 15 16 17 18 19 20 21 22 23 24 25 26 27 28 29 30 31 32 33 34 35 36 37 38 39 40 C-T			
7.	N-T 01 02 03 04 05 06 07 08 09 10 11 12 13 14 15 16 17 18 19 20 21 22 23 24 25 26 27 28 29 30 31 32 33 34 35 36 37 38 39 40 C-T			
8.	N-T 01 02 03 04 05 06 07 08 09 10 11 12 13 14 15 16 17 18 19 20 21 22 23 24 25 26 27 28 29 30 31 32 33 34 35 36 37 38 39 40 C-T			
9.	N-T 01 02 03 04 05 06 07 08 09 10 11 12 13 14 15 16 17 18 19 20 21 22 23 24 25 26 27 28 29 30 31 32 33 34 35 36 37 38 39 40 C-T			
10.	N-T 01 02 03 04 05 06 07 08 09 10 11 12 13 14 15 16 17 18 19 20 21 22 23 24 25 26 27 28 29 30 31 32 33 34 35 36 37 38 39 40 C-T			

D. SPOT SPECIFICATION:

☐ Small ☐ Large
☐ Uncleaved ☐ Cleaved

E. MEMBRANE TYPE:

☐ Commercial ☐ CAPE
☐ Beta-Ala ☐ TOTD
☐ Others: _____

F. NUMBER OF COPIES:
State the number of copies of the array.

_____

G. PEPTIDE TYPE:

☐ Linear
☐ C-C-cyclic
☐ Amide cyclic

H. PEPTIDE AMINO ACIDS:

☐ L-amino acids ☐ L- and D amino acids
☐ D-amino acids ☐ Omit cysteine
☐ Other specification: _____

I. N-TERMINUS:

☐ Free amino group
☐ Acetylated
☐ Other modification: _____

J. PROBING INCUBATION:

1st incubation (Sample): _____

_____

2nd incubation (Detection: _____

_____

Detection method: _____

K. CONTROL INCUBATION:

1st incubation (Sample): _____

_____

2nd incubation (Detection: _____

_____

Detection method: _____

L. REMARKS:

_____

_____

Name of person completing this form *Email Address/Facsimile Number/ Phone Number* *Date (y/m/d)*

KINEXUS

Form: CPAP3-SIF

KINEXUS ORDER NUMBER
For Kinexus internal use only.

CUSTOM PEPTIDE ARRAY PRODUCTION

PRELIMINARY

SERVICE IDENTIFICATION FORM

Subject to terms of the Kinexus Proteomics Services Agreement

NAME: **COMPANY/INSTITUTE:**

(Authorized Representative or Principal Investigator)

Particulars of Service Requested:

Please refer to the CPAP Services Customer Information Package for further details about these services. Complete the sections and check the boxes as appropriate. Blue areas are for Kinexus use only and should not be filled. An electronic fillable copy of this form is available from Kinexus. If you need assistance completing this form, contact Dr. Dirk Winkler by calling toll free in North America 1-866-KINEXUS (866-546-3987) or by email at peptides@kinexus.ca.

A. CUSTOM SERVICE REQUESTED:

☐ **Truncation Analysis (CPAP3)**

Systematic reduction of the peptide length with given sequence (wild-type) up to a length of 3 amino acids synthesized on a cellulose membrane.

KINEXUS ID NUMBER
(Bar Code Identification Number)
For Kinexus internal use only.

B. CPAP3-SIF IDENTIFICATION NAME:

Client ID: _____

Use this ID name of your choice for your internal reference and completion of the CPAP-SOF form.

C.	DESCRIPTION: Amino Acid Sequence (Wild-type)	Array Name (Not required)	Product Code Kinexus use only.	Cost U.S. $ Kinexus use only.
1.	N-T 01 02 03 04 05 06 07 08 09 10 11 12 13 14 15 16 17 18 19 20 21 22 23 24 25 26 27 28 29 30 31 32 33 34 35 36 37 38 39 40 C-T	_____		
2.	N-T 01 02 03 04 05 06 07 08 09 10 11 12 13 14 15 16 17 18 19 20 21 22 23 24 25 26 27 28 29 30 31 32 33 34 35 36 37 38 39 40 C-T	_____		
3.	N-T 01 02 03 04 05 06 07 08 09 10 11 12 13 14 15 16 17 18 19 20 21 22 23 24 25 26 27 28 29 30 31 32 33 34 35 36 37 38 39 40 C-T	_____		
4.	N-T 01 02 03 04 05 06 07 08 09 10 11 12 13 14 15 16 17 18 19 20 21 22 23 24 25 26 27 28 29 30 31 32 33 34 35 36 37 38 39 40 C-T	_____		
5.	N-T 01 02 03 04 05 06 07 08 09 10 11 12 13 14 15 16 17 18 19 20 21 22 23 24 25 26 27 28 29 30 31 32 33 34 35 36 37 38 39 40 C-T	_____		
6.	N-T 01 02 03 04 05 06 07 08 09 10 11 12 13 14 15 16 17 18 19 20 21 22 23 24 25 26 27 28 29 30 31 32 33 34 35 36 37 38 39 40 C-T	_____		
7.	N-T 01 02 03 04 05 06 07 08 09 10 11 12 13 14 15 16 17 18 19 20 21 22 23 24 25 26 27 28 29 30 31 32 33 34 35 36 37 38 39 40 C-T	_____		
8.	N-T 01 02 03 04 05 06 07 08 09 10 11 12 13 14 15 16 17 18 19 20 21 22 23 24 25 26 27 28 29 30 31 32 33 34 35 36 37 38 39 40 C-T	_____		
9.	N-T 01 02 03 04 05 06 07 08 09 10 11 12 13 14 15 16 17 18 19 20 21 22 23 24 25 26 27 28 29 30 31 32 33 34 35 36 37 38 39 40 C-T	_____		
10.	N-T 01 02 03 04 05 06 07 08 09 10 11 12 13 14 15 16 17 18 19 20 21 22 23 24 25 26 27 28 29 30 31 32 33 34 35 36 37 38 39 40 C-T	_____		

D. SPOT SPECIFICATION:

☐ Small ☐ Large
☐ Uncleaved ☐ Cleaved

E. MEMBRANE TYPE:

☐ Commercial ☐ CAPE
☐ Beta-Ala ☐ TOTD
☐ Others: _____

F. NUMBER OF COPIES:
State the number of copies of the array.

_____

G. PEPTIDE TYPE:

☐ Linear
☐ C-C-cyclic
☐ Amide cyclic

H. TRUNCATION:

☐ From N terminus only
☐ From C terminus only
☐ From both sides

I. N-TERMINUS:

☐ Free amino group
☐ Acetylated
☐ Other modification:

_____

J. PROBING INCUBATION:

1st incubation (Sample): _____

2nd incubation (Detection: _____

Detection method: _____

K. CONTROL INCUBATION:

1st incubation (Sample): _____

2nd incubation (Detection: _____

Detection method: _____

L. REMARKS:

_____

_____

Name of person completing this form *Email Address/Facsimile Number/ Phone Number* *Date (y/m/d)*

CUSTOM PEPTIDE ARRAY PRODUCTION

PRELIMINARY

SERVICE IDENTIFICATION FORM

Subject to terms of the Kinexus Proteomics Services Agreement

Form: CPAP4-SIF

KINEXUS ORDER NUMBER
For Kinexus internal use only.

NAME: **COMPANY/INSTITUTE:**

(Authorized Representative or Principal Investigator)

Particulars of Service Requested:

Please refer to the CSPP Services Customer Information Package for further details about these services. Complete the sections and check the boxes as appropriate. Areas indicated in light blue are for Kinexus use only and should not be filled. An electronic fillable copy of this form is available from the Kinexus website and by e-mail. If you need assistance completing this form, contact Dr. Dirk Winkler by calling toll free in North America 1-866-KINEXUS (866-546-3987) or by email at peptides@kinexus.ca.

A. CUSTOM SERVICE REQUESTED:

☐ **Random Peptide Library (CPAP4)**

Synthesis of a library of random generated peptides on a cellulose membrane.

KINEXUS ID NUMBER
(Bar Code Identification Number)
For Kinexus internal use only.

B. CPAP4-SIF IDENTIFICATION NAME:

Client ID: _____

Use this ID name of your choice for your internal reference and completion of the CPAP-SOF form.

C. ARRAY NAME: (Not required)

Product Code
Kinexus use only.

Cost U.S. $
Kinexus use only.

D. SPOT SPECIFICATION:

☐ Small ☐ Large
☐ Uncleaved ☐ Cleaved

E. MEMBRANE TYPE:

☐ Commercial ☐ CAPE
☐ Beta-Ala ☐ TOTD
☐ Others: _____

F. NUMBER OF COPIES:
State the number of copies of the array.

_____

G. PEPTIDE TYPE:

☐ Linear
☐ C-C-cyclic
☐ Amide cyclic

H. PEPTIDE AMINO ACIDS:

☐ L-amino acids ☐ Omit Cys
☐ D-amino acids ☐ Omit Trp
☐ D- and L- aa ☐ Omit Cys and Trp
☐ Other specification: _____

I. N-TERMINUS:

☐ Free amino group
☐ Acetylated
☐ Other modification:
_____

J. PROBING INCUBATION:

1st incubation (Sample): _____

2nd incubation (Detection: _____

Detection method: _____

K. CONTROL INCUBATION:

1st incubation (Sample): _____

2nd incubation (Detection: _____

Detection method: _____

L. PEPTIDE INFO:

Length of desired peptides: _____ aa

Number of peptides: _____

M. REMARKS: _____

_____

Name of person completing this form *Email Address/Facsimile Number/ Phone Number* *Date (y/m/d)*

KINEXUS

Form: CPAP5-SIF

KINEXUS ORDER NUMBER
For Kinexus internal use only.

CUSTOM PEPTIDE ARRAY PRODUCTION

PRELIMINARY

SERVICE IDENTIFICATION FORM

Subject to terms of the Kinexus Proteomics Services Agreement

NAME: **COMPANY/INSTITUTE:**

(Authorized Representative or Principal Investigator)

Particulars of Service Requested:

Please refer to the CSPP Services Customer Information Package for further details about these services. Complete the sections and check the boxes as appropriate. Areas indicated in light blue are for Kinexus use only and should not be filled. An electronic fillable copy of this form is available from the Kinexus website and by e-mail. If you need assistance completing this form, contact Dr. Dirk Winkler by calling toll free in North America 1-866-KINEXUS (866-546-3987) or by email at peptides@kinexus.ca.

A. CUSTOM SERVICE REQUESTED:

☐ **Combinatorial Peptide Library (CPAP5)**

Synthesis of a library of peptides on a cellulose membrane organized in a combinatorial approach.

KINEXUS ID NUMBER
(Bar Code Identification Number)
For Kinexus internal use only.

B. CPAP5-SIF IDENTIFICATION NAME:

Client ID: _____

Use this ID name of your choice for your internal reference and completion of the CPAP-SOF form.

C. ARRAY NAME: _____ (Not required)

Product Code
Kinexus use only.

Cost U.S. $
Kinexus use only.

D. SPOT SPECIFICATION:

☐ Small ☐ Large
☐ Uncleaved ☐ Cleaved

E. MEMBRANE TYPE:

☐ Commercial ☐ CAPE
☐ Beta-Ala ☐ TOTD
☐ Others: _____

F. NUMBER OF COPIES:
State the number of copies of the array.

_____

G. PEPTIDE TYPE:

☐ Linear
☐ C-C-cyclic
☐ Amide cyclic

H. PEPTIDE AMINO ACIDS:

☐ L-amino acids ☐ Omit Cys
☐ D-amino acids ☐ Omit Trp
☐ D- and L- aa ☐ Omit Cys and Trp
☐ Other specification: _____

I. N-TERMINUS:

☐ Free amino group
☐ Acetylated
☐ Other modification:
_____

J. PROBING INCUBATION:

1st incubation (Sample): _____
_____
2nd incubation (Detection: _____
_____
Detection method: _____

K. CONTROL INCUBATION:

1st incubation (Sample): _____
_____
2nd incubation (Detection: _____
_____
Detection method: _____

L. PEPTIDE INFO:

Length of desired peptides: _____ aa

Number of peptides: _____

Est. number deconvolutions: _____ (Kinexus only)

M. REMARKS:

_____
_____
_____

Name of person completing this form *Email Address/Facsimile Number/ Phone Number* *Date (y/m/d)*

KINEXUS

Form: CPAP6-SIF

KINEXUS ORDER NUMBER
For Kinexus internal use only.

CUSTOM PEPTIDE ARRAY PRODUCTION

PRELIMINARY

SERVICE IDENTIFICATION FORM

Subject to terms of the Kinexus Proteomics Services Agreement

NAME: **COMPANY/INSTITUTE:**

(Authorized Representative or Principal Investigator)

Particulars of Service Requested:

Please refer to the CSPP Services Customer Information Package for further details about these services. Complete the sections and check the boxes as appropriate. Areas indicated in light blue are for Kinexus use only and should not be filled. An electronic fillable copy of this form is available from the Kinexus website and by e-mail. If you need assistance completing this form, contact Dr. Dirk Winkler by calling toll free in North America 1-866-KINEXUS (866-546-3987) or by email at peptides@kinexus.ca.

A. CUSTOM SERVICE REQUESTED:

☐ **Cluster Peptide Library (CPAP6)**

Synthesis of a library of selected peptides on a cellulose membrane with clusters of amino acids.

KINEXUS ID NUMBER
(Bar Code Identification Number)
For Kinexus internal use only.

B. CPAP6-SIF IDENTIFICATION NAME:

Client ID: _____

Use this ID name of your choice for your internal reference and completion of the CPAP-SOF form.

C. ARRAY NAME: (Not required)

Product Code
Kinexus use only.

Cost U.S. $
Kinexus use only.

D. SPOT SPECIFICATION:

☐ Small ☐ Large
☐ Uncleaved ☐ Cleaved

E. MEMBRANE TYPE:

☐ Commercial ☐ CAPE
☐ Beta-Ala ☐ TOTD
☐ Others: _____

F. NUMBER OF COPIES:
State the number of copies of the array.

_____

G. PEPTIDE TYPE:

☐ Linear
☐ C-C-cyclic
☐ Amide cyclic

H. PEPTIDE AMINO ACIDS:

☐ L-amino acids ☐ Omit Cys
☐ D-amino acids ☐ Omit Trp
☐ D- and L- aa ☐ Omit Cys and Trp
☐ Other specification: _____

I. N-TERMINUS:

☐ Free amino group
☐ Acetylated
☐ Other modification:
_____

J. PROBING INCUBATION:

1st incubation (Sample): _____
_____
2nd incubation (Detection: _____
_____
Detection method: _____

K. CONTROL INCUBATION:

1st incubation (Sample): _____
_____
2nd incubation (Detection: _____
_____
Detection method: _____

L. PEPTIDE INFO:

Length of desired peptides: _____ aa

Number of peptides: _____

Est. number deconvolutions: _____ (Kinexus only)

M. REMARKS:

_____
_____
_____

Name of person completing this form *Email Address/Facsimile Number/ Phone Number* *Date (y/m/d)*

KINEXUS

Form: CPAP7-SIF

KINEXUS ORDER NUMBER
For Kinexus internal use only.

CUSTOM PEPTIDE ARRAY PRODUCTION

PRELIMINARY

SERVICE IDENTIFICATION FORM

Subject to terms of the Kinexus Proteomics Services Agreement

NAME: **COMPANY/INSTITUTE:**

(Authorized Representative or Principal Investigator)

Particulars of Service Requested:

Please refer to the CSPP Services Customer Information Package for further details about these services. Complete the sections and check the boxes as appropriate. Areas indicated in light blue are for Kinexus use only and should not be filled. An electronic fillable copy of this form is available from the Kinexus website and by e-mail. If you need assistance completing this form, contact Dr. Dirk Winkler by calling toll free in North America 1-866-KINEXUS (866-546-3987) or by email at peptides@kinexus.ca.

A. CUSTOM SERVICE REQUESTED:

☐ **Loop Scan (Cysteine Scan) (CPAP7)**

Systematic exchange of 2 amino acids of a given peptide sequence (wild-type) by 2 cysteines or their insertion and the consecutive cyclization synthesized on a cellulose membrane.

KINEXUS ID NUMBER
(Bar Code Identification Number)
For Kinexus internal use only.

B. CPAP7-SIF IDENTIFICATION NAME:

Client ID: _____

Use this ID name of your choice for your internal reference and completion of the CPAP-SOF form.

C.	DESCRIPTION: Amino Acid Sequence (Wild-type)	Peptide Name (Not required)	Product Code Kinexus use only.	Cost U.S. $ Kinexus use only.
1.	N-T 01 02 03 04 05 06 07 08 09 10 11 12 13 14 15 16 17 18 19 20 21 22 23 24 25 26 27 28 29 30 31 32 33 34 35 36 37 38 39 40 C-T			
2.	N-T 01 02 03 04 05 06 07 08 09 10 11 12 13 14 15 16 17 18 19 20 21 22 23 24 25 26 27 28 29 30 31 32 33 34 35 36 37 38 39 40 C-T			
3.	N-T 01 02 03 04 05 06 07 08 09 10 11 12 13 14 15 16 17 18 19 20 21 22 23 24 25 26 27 28 29 30 31 32 33 34 35 36 37 38 39 40 C-T			
4.	N-T 01 02 03 04 05 06 07 08 09 10 11 12 13 14 15 16 17 18 19 20 21 22 23 24 25 26 27 28 29 30 31 32 33 34 35 36 37 38 39 40 C-T			
5.	N-T 01 02 03 04 05 06 07 08 09 10 11 12 13 14 15 16 17 18 19 20 21 22 23 24 25 26 27 28 29 30 31 32 33 34 35 36 37 38 39 40 C-T			
6.	N-T 01 02 03 04 05 06 07 08 09 10 11 12 13 14 15 16 17 18 19 20 21 22 23 24 25 26 27 28 29 30 31 32 33 34 35 36 37 38 39 40 C-T			
7.	N-T 01 02 03 04 05 06 07 08 09 10 11 12 13 14 15 16 17 18 19 20 21 22 23 24 25 26 27 28 29 30 31 32 33 34 35 36 37 38 39 40 C-T			
8.	N-T 01 02 03 04 05 06 07 08 09 10 11 12 13 14 15 16 17 18 19 20 21 22 23 24 25 26 27 28 29 30 31 32 33 34 35 36 37 38 39 40 C-T			
9.	N-T 01 02 03 04 05 06 07 08 09 10 11 12 13 14 15 16 17 18 19 20 21 22 23 24 25 26 27 28 29 30 31 32 33 34 35 36 37 38 39 40 C-T			
10.	N-T 01 02 03 04 05 06 07 08 09 10 11 12 13 14 15 16 17 18 19 20 21 22 23 24 25 26 27 28 29 30 31 32 33 34 35 36 37 38 39 40 C-T			

D. SPOT SPECIFICATION:

☐ Small ☐ Large
☐ Uncleaved ☐ Cleaved

E. MEMBRANE TYPE:

☐ Commercial ☐ CAPE
☐ Beta-Ala ☐ TOTD
☐ Others: _____

F. NUMBER OF COPIES:

State the number of copies of the array.

_____

G. N-TERMINUS:

☐ Free amino group
☐ Acetylated
☐ Other modification: _____

H. PROBING INCUBATION:

1st incubation (Sample): _____

2nd incubation (Detection: _____

Detection method:

I. CONTROL INCUBATION:

1st incubation (Sample): _____

2nd incubation (Detection: _____

Detection method:

J. REMARKS:

_____

_____

Name of person completing this form *Email Address/Facsimile Number/ Phone Number* *Date (y/m/d)*

CUSTOM PEPTIDE ARRAY PRODUCTION

PRELIMINARY

SERVICE IDENTIFICATION FORM

Subject to terms of the Kinexus Proteomics Services Agreement

Form: CPAP8-SIF

KINEXUS ORDER NUMBER
For Kinexus internal use only.

NAME: **COMPANY/INSTITUTE:**

(Authorized Representative or Principal Investigator)

Particulars of Service Requested:

Please refer to the CPAP Services Customer Information Package for further details about these services. Complete the sections and check the boxes as appropriate. Blue areas are for Kinexus use only and should not be filled. An electronic fillable copy of this form is available from Kinexus. If you need assistance completing this form, contact Dr. Dirk Winkler by calling toll free in North America 1-866-KINEXUS (866-546-3987) or by email at peptides@kinexus.ca.

A. CUSTOM SERVICE REQUESTED:	**KINEXUS ID NUMBER**	**B. CPAP8-SIF IDENTIFICATION NAME:**
☐ **Selected (Customized) Library (CPAP8)** Synthesis of a set of given peptides on a cellulose membrane.	*(Bar Code Identification Number)* For Kinexus internal use only.	Client ID: _____ *Use this ID name of your choice for your internal reference and completion of the CPAP-SOF form.*

C.	AMINO ACID SEQUENCES: Provide a list with the desired amino acid sequences of the requested peptides as an attachment.	Product Code Kinexus use only.	Cost U.S. $ Kinexus use only.
1.	File name for attachment with peptides sequences: _____		

D. SPOT SPECIFICATION:	E. MEMBRANE TYPE:	F. NUMBER OF COPIES:	G. N-TERMINUS:
☐ Small ☐ Large ☐ Uncleaved ☐ Cleaved	☐ Commercial ☐ CAPE ☐ Beta-Ala ☐ TOTD ☐ Others: _____	State the number of copies of the array. _____	☐ Free amino group ☐ Acetylated ☐ Other modification: _____

H. PEPTIDE INFO:	I. PROBING INCUBATION:	J. CONTROL INCUBATION:
Length of desired peptides: _____ aa Number of peptides: _____	1st incubation (Sample): _____ 2nd incubation (Detection: _____ Detection method: _____	1st incubation (Sample): _____ 2nd incubation (Detection: _____ Detection method: _____

K. REMARKS:

_____

_____

Name of person completing this form *Email Address/Facsimile Number/ Phone Number* *Date (y/m/d)*

KINEXUS

Form: CPAPA-SIF

KINEXUS ORDER NUMBER
For Kinexus internal use only.

CUSTOM PEPTIDE ARRAY PRODUCTION

PRELIMINARY

SERVICE IDENTIFICATION FORM

Subject to terms of the Kinexus Proteomics Services Agreement

NAME: **COMPANY/INSTITUTE:**

(Authorized Representative or Principal Investigator)

Particulars of Service Requested:

Please refer to the CSPP Services Customer Information Package for further details about these services. Complete the sections and check the boxes as appropriate. Areas indicated in light blue are for Kinexus use only and should not be filled. An electronic fillable copy of this form is available from the Kinexus website and by e-mail. If you need assistance completing this form, contact Dr. Dirk Winkler by calling toll free in North America 1-866-KINEXUS (866-546-3987) or by email at peptides@kinexus.ca.

A. CUSTOM SERVICE REQUESTED:	**KINEXUS ID NUMBER**	**B. CPAPA-SIF IDENTIFICATION NAME:**
☐ **CelluSpots™ Custom Peptide Array (CPAPA)** Synthesis of Cellupots™ arrays of a set of given linear peptides on glass slides.	*(Bar Code Identification Number)* For Kinexus internal use only.	Client ID: _____ *Use this ID name of your choice for your internal reference and completion of the CPAP-SOF form.*

C.	AMINO ACID SEQUENCES: Provide a list with the desired amino acid sequences of the requested peptides as an attachment.	Product Code Kinexus use only.	Cost U.S. $ Kinexus use only.
1.	File name for attachment with peptides sequences: _____		

D. ARRAY PRODUCT NAME:	E. MEMBRANE TYPE:	F. N-TERMINUS:	G. NUMBER OF GLASS SLIDES:	H. PEPTIDE INFO:
Provide a name for the array. This can be the same as the Client ID Name. _____	☐ Commercial ☐ CAPE ☐ Beta-Ala ☐ TOTD ☐ Others: _____	☐ Free amino group ☐ Acetylated ☐ Other modification: _____	☐ 20 slides ☐ 40 slides ☐ 60 slides ☐ >60 slides	Length of desired peptides: _____ aa Number of peptides: _____

I. REMARKS:

_____

_____

Name of person completing this form *Email Address/Facsimile Number/ Phone Number* *Date (y/m/d)*

KINEXUS

Form: CPAPB-SIF

KINEXUS ORDER NUMBER
For Kinexus internal use only.

CUSTOM PEPTIDE ARRAY PRODUCTION

PRELIMINARY

SERVICE IDENTIFICATION FORM

Subject to terms of the Kinexus Proteomics Services Agreement

NAME: **COMPANY/INSTITUTE:**

(Authorized Representative or Principal Investigator)

Particulars of Service Requested:

Please refer to the CSPP Services Customer Information Package for further details about these services. Complete the sections and check the boxes as appropriate. Areas indicated in light blue are for Kinexus use only and should not be filled. An electronic fillable copy of this form is available from the Kinexus website and by e-mail. If you need assistance completing this form, contact Dr. Dirk Winkler by calling toll free in North America 1-866-KINEXUS (866-546-3987) or by email at peptides@kinexus.ca.

A. CUSTOM SERVICE REQUESTED:	**KINEXUS ID NUMBER**	**B. CPAPB-SIF IDENTIFICATION NAME:**
☐ **CelluSpots™ Kinase Substrate Array (CPAPB)** Synthesis of Cellupots™ arrays on glass slides of a set of given kinase substrate peptides from annotated phosphorylation sites.	*(Bar Code Identification Number)* For Kinexus internal use only.	Client ID: _____ *Use this ID name of your choice for your internal reference and completion of the CPAP-SOF form.*

C. PRODUCT DESCRIPTION:			Product Code Kinexus use only.	Cost U.S. $ Kinexus use only.
Array	**Unique Spots per Slide**	**# Slides**		
Protein-tyrosine Kinase Substrates (1 array)	384 in duplicate	Pack of ___		
Protein-serine/threonine Kinase Substrates I + II (2 arrays)	384 in duplicate	Pack of ___ pairs		
Test Packs				
Protein-tyrosine Kinase I Plus (one slide)	384 in duplicate	☐ 2 duplicate		
Protein-serine/threonine Kinase Substrates I + II (two slides)	384 in duplicate	☐ 1 pair		

D. REMARKS:

_____

_____

Name of person completing this form *Email Address/Facsimile Number/ Phone Number* *Date (y/m/d)*

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: _____

_____

_____

R E C I T A L S

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.

_____	**KINEXUS BIOINFORMATICS CORPORATION**
Printed Name of Institute or Company	
Per: _____	Per: _____
Signature of Authorized Representative	*Signature of Dr. Steven Pelech*
Name: _____	**Dr. Steven Pelech**
Printed Name of Authorized Representative	
Title: _____	**President and Chief Scientific Officer**
Printed Title of Authorized Representative	
Date signed: _____	Date signed: _____