KINEXUS

CKSP SERVICES

Version 10JA20

CUSTOM SERVICES

KINASE-SUBSTRATE PROFILING
CUSTOMER INFORMATION PACKAGE

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CUSTOM KINASE SUBSTRATE PROFILING

1. INTRODUCTION

The vast majority of the proteins phosphorylated by specific protein kinases in humans and other species remain unknown despite more than 40 years of intense effort. However, with the emergence of protein kinases as one of the most promising families of drug targets in the pharmaceutical industry today, it is critical to define the proteins that are controlled by these important regulatory enzymes. Our Custom Kinase Substrate Profiling Service uniquely permits the rapid simultaneous identification of a panel of physiological substrates for most known protein kinases in any tissues or cells of specific interest. Our cost effective strategy also provides for the identification of the specific sites at which these substrates are phosphorylated, as well as commercial antibodies that can be used to specifically track and quantify these phospho-sites in follow up studies. Our methodology is superior to any other procedures that have been applied to kinase substrate identification including mass spectrometry and peptide and protein microarrays, which are more expensive to perform and do not define reagents for follow on experiments. With our flexible and convenient protein kinase substrate identification service, clients can send us their own kinases and cell/tissue lysates or they can choose from our collections of over 360 active human kinases, and lysates from 14 of the most commonly studied human tumour cell lines. Within four weeks of receipt of a client order, Kinexus will provide information about a large panel of potential substrates as revealed with a 270+ phospho-site antibody microarray and validation studies with 18 of the most promising leads by immunoblotting. The selection of the candidate phospho-sites for the Western blotting exploits proprietary information that Kinexus has developed to determine negative and positive determinants for specific kinase substrate recognition. The results from this unique service can be used to define signalling pathways impacted by specific kinases, identify reagents to enable kinase inhibitor discovery *in vitro*, and ascertain the effectiveness and specificity of kinase inhibitor drugs in living systems.

The PhosphoNET Knowledgebase, soon to become available on-line from Kinexus, features over 24,000 phospho-sites in over 8000 human proteins. However, it appears that over 500,000 phospho-sites are likely to exist, and with 516 known human protein kinases, each kinase appears to target about 1000 phospho-sites on average. At this juncture, for more than half of the human protein kinases, not a single physiological substrate has been reported in the scientific literature. Furthermore, for about a third of the remaining human protein kinases, only one or two phosphoprotein substrates have been identified. A comprehensive understanding of the composition and architecture of cell signalling networks will require a much deeper knowledge of which phosphoproteins and which of their phospho-sites are targeted by specific protein kinases, and what are the physiological consequences of their phosphorylation.

Most of the known phosphorylation sites have been elucidated through tandem MS-MS mass spectrometry. This powerful and sensitive method relies on phosphoprotein enrichment techniques such as strong cation exchange chromatography and can permit identification of hundreds of phosphosites at once. However, this method is not very quantitative, and it is impractical and costly for routine analysis of phosphorylation changes in tissues and cells that are often limiting in quantity. Moreover, with a novel phosphorylation site defined by mass spectrometry it can take more than 6 months at high expense to develop a reliable phospho-site-specific antibody for its detection by immunoblotting and immunohistochemistry. With the availability of several hundred commercial antibodies from several vendors, Kinexus has reversed the paradigm for phospho-site discovery with its Kinex™ antibody microarray and Kinetworks™ multi-immunoblotting services. With these methodologies, Kinexus uses panels of phospho-site antibodies to detect known and cross-reactive proteins that display altered phosphorylation in living systems in response to hormonal and pharmacological manipulations or, as with our Custom Kinase Substrate Profiling Service, increased phosphorylation *in vitro* with purified kinases. Any cross-reactive proteins can be easily enriched with the detecting phospho-site antibody and identified by MALDI mass spectrometry. Moreover, since the phospho-site epitope of the detection antibody is known, it is often easy to locate the affected phosphorylation site without further sequencing. Thus antibody-driven phosphoprotein discovery is highly cost effective, informative and enabling for immediate follow up analyses with other methodologies that exploit antibodies.

Previous services for kinase substrate identification from other companies have relied on the radioactive tagging of known purified proteins or unknown proteins in fractionated cell and tissue lysates with purified protein kinases and [gamma-^{32}P]ATP. Enrichment of phosphoprotein substrates often involves 1D sodium dodecylsulphate gel electrophoresis (SDS-PAGE) or 2D gel electrophoresis. However, these methodologies have severe limitations with respect to separation capacity and the amount of starting material that can be resolved. To identify any specific phospho-sites on purified phosphoproteins, subsequent sequencing is performed by Edman protein sequencing or tandem MS-MS mass spectrometry. As these procedures involve many steps, the risks for artifacts and loss of phosphorylation are very high. Moreover, in view of the required labour and expensive equipment required for these approaches, these strategies are beyond the financial means of most research laboratories. With our Custom Kinase Substrate Profiling Service, for their favourite experimental model system and a kinase supplied by Kinexus, any researcher can have a panel of physiological substrates, the phospho-sites, and detecting phospho-site antibodies identified for less than US$3000 with our non-confidential pricing.

2. SERVICE DESCRIPTION

The Custom Kinase Substrate Profiling (CKSP) Service uses the Kinex™ Antibody Microarray (KAM) to detect the phosphorylation of hundreds of proteins that are present in crude cell and tissue lysates with commercial phospho-site antibodies. The latest version of KAM features over 270 phospho-site antibodies. Clients can provide frozen lysates of cells or tissues for kinase substrate profiling or for an added fee they can select from lysates from the Kinexus inventory, which have been prepared from the following 14 human tumour cell lines.

• A431 - Skin epidermoid carcinoma cells
• A549 - Lung carcinoma cells
• Daudi – B cell lymphoma cells
• HCT116 - Colon carcinoma cells
• HEK 293 - Female fetal kidney cells
• HeLa - Cervix epithelial adenocarcinoma cells
• HepG2 - Liver carcinoma cells
• HL-60 - Peripheral blood promyeloblasts
• HUV-EC - Umbilical vein endothelial cells
• Jurkat - T cell leukemia cells
• MCF-7- Breast epithelial adenocarcinoma cells
• PC-3 - Prostate adenocarcinoma cells
• T98G - Brain glioblastoma cells
• THP1 – Monocyte leukemic cells

These cell lines have been selected on the basis of their broad representation of human tissues and cells, gender and age, and because they are commonly studied as revealed in the scientific literature. More information on these cell lines is provided in Appendix 2. All of these cells lines can be sourced from the American Type Culture Collection for follow up studies. In addition, most of these cell lines have been treated in house at Kinexus with diverse drugs and hormones in time course and dose response studies, and they are available with the Kinex™ Reverse Lysate Microarray Service that is also offered through Kinexus. Consequently, any phosphoprotein that is identified with our CKSP service can be rapidly screened for its regulation in a broad range of other cell lines as well as monkey, rat, mouse and frog tissues with our Kinex™ Reverse Lysate Microarray Service, and further confirmed with our Custom Kinetworks™ Immunoblotting Service with the very same lysates. Moreover, interesting phosphoproteins can be screened *in silico* on-line with our KiNET Database with the quantitative results from over 5000 diverse cell and tissue samples analyzed with our Standard Kinetworks™ Immunoblotting Services. This ability to validate and correlate the findings from our various proteomics services is a unique and distinguishing feature of our powerful platform of integrated proteomics and bioinformatics services.

Clients are able to provide their own preparations of purified protein kinases for use with the CKSP service. Alternatively, for a fee, clients can choose from our growing inventory of over 360 active, human protein kinases as well as more than 60 additional mutant forms of these kinases. A listing of our most recent inventory of these kinases and their prices are provided in Appendix 1. Kinexus sources these protein kinases from other vendors, and the added fee is based on our cost recovery. Consequently, the sliding price scale for these enzymes reflects the purchase price of these kinases by Kinexus. We are pleased to identify the commercial source of each protein kinase that we use upon request.

To identify kinase substrates in cell and tissue lysates, these lysates are incubated in solution the presence of ATP with (treated) and without (control) the purified protein kinase of interest. At the conclusion of the reaction, a portion of the control and treated lysates are subjected to Kinex™ Antibody Microarray analysis and tested for the

increased detection of signal of fluorescent dye-labeled lysate proteins to the capture phospho-antibodies on the microarray. It is presumed that the enhancement of a phospho-site antibody signal on the KAM microarray is due to increased phosphorylation of the target phosphoprotein by the added protein kinase. However, there are other alternative explanations for elevated phosphorylation signals including cross-reactivity with other phosphoproteins, indirect phosphorylation via endogenous protein kinases that are activated by the added kinase, increased protein-protein interactions, and increased protein stability. Consequently, it is critical to confirm protein kinase substrate leads by Western blotting.

Each phospho-site antibody used on the Kinex™ Antibody Microarray has been affinity-purified against a defined phosphorylation site peptide sequence or is a monoclonal antibody. Appendix 3 provides a list of the phospho-site antibodies that are used in the Kinex™ Antibody Microarray. Kinexus uses information about the amino acid sequences of these phosphorylation sites to prioritize those that best match the known consensus recognition sequences of the protein kinase under study. Through bioinformatics, Kinexus has carefully examined hundreds of protein kinases to define positive and negative determinants for substrate recognition by each of these enzymes. With the CKSP Service offered by Kinexus, those phospho-sites antibodies that display sequences that best match the target kinase consensus sequence are considered for further analysis by immunoblotting.

In addition to the criteria of featuring appropriate kinase recognition concensus sequences for selection of phospho-site antibodies for immunoblotting validation, Kinexus also focuses on those phospho-site antibodies that reveal the strong signals and largest increases in phosphorylation in the presence of the added protein kinase. The most promising 18 antibodies are selected for immunoblotting both the control and kinase-treated lysates. Images of these immunoblots are provided to clients, and upon request Kinexus is pleased to reveal the commercial sources of these antibodies.

The immunoblotting results can also reveal novel cross-reactive phosphoproteins that serve as protein kinase substrates. Such proteins can usually be identified following immunoprecipitation, resolution by SDS-PAGE and MALDI mass spectrometry. If clients require help for identification of intriguing cross-reactive proteins, Kinexus is pleased to assist. Clients should enquire with our technical service representatives for the costs for custom services for identification of cross-reactive proteins by mass spectrometry.

On the next page, Figure 1 provides an overview of how the various proteomics and bioinformatics services integrate in the provision of the Custom Kinase Substrate Profiling Service. It also presents the options for clients to use their own kinases or cell and tissues lysates, or to source these from Kinexus. In addition to some of the previously mentioned services, we also offer several other supporting services that permit our clients to further follow up on their results. These include our custom Kinetworks™ Immunoblotting Services, our IHC Immunohistochemistry Services, and our Custom Graphics Services. Our Custom Kinetworks™ KCSS 1.0 Service allows clients to choose *any* 3 target proteins (of different molecular weight) to be quantified for phosphorylation changes in 8 different samples side-by-side on the same immunoblot. Our technical service representatives are pleased to discuss how you can best take advantage of your results from our various services in the most cost effective way.

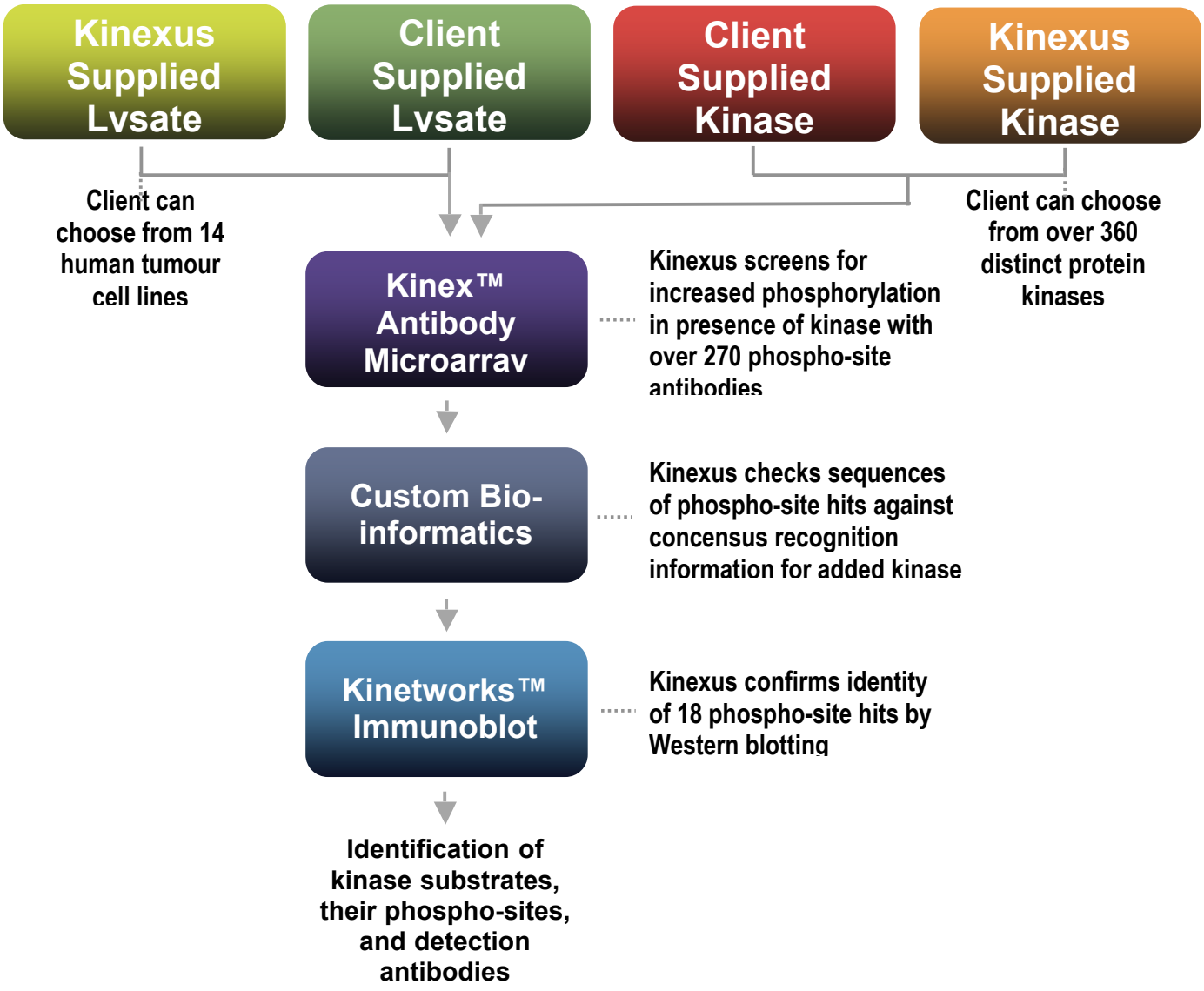


Figure 1. Overview of Custom Kinase Substrate Profiling Service from Kinexus.

3. EXAMPLES OF PROTEIN KINASE SUBSTRATE IDENTIFICATIONS

To illustrate the power of our Custom Kinase Substrate Profiling Service, we have provided two examples with well known protein kinases in this section of this Customer Information Package. Additional examples with two other well characterized kinases (i.e. cAMP-dependent Protein Kinase (PKA) and Src) are provided at the end of this Package. The cell lysates used for these studies were obtained from the HeLa human cervical carcinoma cell line.

Table 1 provides the results of Kinex™ Antibody Microarray analysis with the Extracellular Regulated Kinase 2 (ERK2) and Cyclin-dependent Kinase 5 (CDK5), which are known proline-directed protein-serine/threonine kinases.

Site Type	STY	STY	STY	ST	ST	ST	Y	Y	Y
%CFC	No. P-Ab ≥25	No. P-Ab ≥50	No. P-Ab ≥100	No. P-Ab ≥25	No. P-Ab ≥50	No. P-Ab ≥100	No. P-Ab ≥25	No. P-Ab ≥50	No. P-Ab ≥100
ERK2	62	26	9	45	18	6	17	8	3
CDK5	69	25	8	48	21	7	12	4	1

Number of Phospho-site Antibodies Showing Increased Phosphorylation with Addition of Kinase

Table 1. Detection of increased phosphorylation with addition of ERK2 and CDK5 to HeLa cell lysates as revealed with the Kinex™ KAM-1.1 antibody microarray with 270 phospho-site antibodies (P-Ab). The percentage change from control (%CFC) with the addition of the protein kinase is shown. S, T and Y corresponds to phospho-sites antibodies developed for serine (S), threonine (T) and tyrosine (Y) phosphorylation sites.

Inspection of Table 1 reveals that 23-24% of the phospho-site antibodies on the KAM-1.1 antibody microarray showed increased phosphorylation of 25% or more in the presence of the added protein kinase, and about 3% displayed increases greater than 2-fold. Approximately 17% and 27% of the observed increases in phosphorylation with CDK5 and ERK2, respectively, were observed with phospho-tyrosine-specific antibodies. However, these protein-serine/threonine kinases are not known to phosphorylate proteins on tyrosine residues. Therefore, in these cases, the increased phosphorylation is likely to be directed at serine and threonine phosphorylation sites on other cross-reactive proteins that feature similar antigenic determinants for the amino acids surrounding the phosphorylation sites with the target sequences for these putative phospho-tyrosine site-specific antibodies.

Tables 2 and 3 provide kinase phosphorylation site concensus recognition matrices that have been developed by Kinexus based on the analysis of 250 and 70 known substrate phosphorylation sites for ERK2 and CDK5, respectively. In these matrices, positive and negative determinants for these kinases are defined by the expected occurrence of each of the 20 common amino acids in each position surrounding the phosphorylation sites after the calculated random occurrence of each type of amino acid at the protein surface has been compensated for. The “0” position corresponds to the location of the phosphorylated amino acid, and for this position the random occurrence of each of the 20 common amino acids has not been deducted. We used this information to identify the presence of strong and moderate positive determinants in the candidate phosphorylation sites that were identified from the Kinex™ KAM-1.1 antibody microarray analyses for these kinases.

AA	(-7)	(-6)	(-5)	(-4)	(-3)	(-2)	(-1)	0	1	2	3	4	5	6	7
Type	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15
A	0	2	-2	-2	1	1	3	0	-6	-1	1	-2	-1	0	1
C	0	0	0	0	0	0	0	0	-1	1	0	-1	1	-1	-1
D	-2	-2	-4	-2	-3	-3	-5	0	-7	-5	-4	-2	-3	-4	0
E	-1	-1	-3	-2	-3	-7	-6	0	-9	-5	-5	-5	-5	-7	-4
F	1	2	2	0	1	-1	1	0	-2	0	3	1	3	3	2
G	0	1	0	0	1	-4	3	0	-7	3	-1	1	-1	0	0
H	0	0	0	-1	0	-1	0	0	-2	-1	2	1	0	0	-1
I	1	1	2	-1	0	1	1	0	-3	1	-2	1	0	0	0
K	0	-4	-3	-1	-3	-4	-1	0	-6	-2	-2	-2	-4	-2	-4
L	-3	-3	1	1	0	5	6	0	-7	1	1	1	-1	1	-2
M	1	2	1	1	0	-1	4	0	-1	1	0	2	1	2	2
N	4	2	2	2	-1	-2	-1	0	-3	1	-1	0	-1	2	1
P	5	2	6	4	7	29	1	0	85	5	4	3	7	3	3
Q	2	0	-2	-1	0	-2	0	0	-3	0	3	0	-2	-1	-2
R	-5	-6	-3	-5	-4	-4	-2	0	-8	0	-2	-5	-2	-2	-2
S	-1	1	3	2	1	-5	-3	68	-11	-2	-1	2	4	3	0
T	3	2	1	5	2	-1	0	31	-5	5	1	5	1	2	3
V	-3	0	-1	1	0	-1	-1	0	-5	0	1	-1	-1	0	1
W	0	-1	-1	-1	-1	-1	-1	0	-1	-1	-1	-1	0	-1	-1
Y	-1	0	0	0	0	-1	0	0	-2	0	1	0	2	1	2

Table 2. Percent amino acid frequency from random surrounding 250 ERK2 phosphorylation sites.

AA	(-7)	(-6)	(-5)	(-4)	(-3)	(-2)	(-1)	0	1	2	3	4	5	6	7
Type	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15
A	0	-1	2	-1	7	0	3	0	-7	-3	-6	0	-1	9	-1
C	0	-1	-1	-1	0	-1	-1	0	-1	-1	-1	0	-1	-1	2
D	-3	-6	-3	3	-4	-3	-6	0	-7	-7	-4	-3	-6	0	0
E	-3	2	-3	-5	-2	-8	-8	0	-9	-6	-9	-6	-6	0	-6
F	-2	-2	-1	-1	2	-1	-1	0	-2	-1	-1	-2	-1	1	-2
G	3	3	-4	-1	2	-6	-1	0	-7	9	-6	-1	7	-3	-3
H	1	1	1	-2	1	-1	-2	0	-2	-1	7	-1	-2	-1	1
I	0	1	1	3	-3	1	0	0	-3	1	0	0	1	-3	-3
K	0	1	3	0	0	-2	5	0	-6	1	17	4	7	5	-2
L	2	-1	-3	0	0	-1	6	0	-7	-3	-6	0	-3	-3	2
M	3	-1	3	-1	-1	0	2	0	-1	-1	-1	2	2	3	2
N	0	1	3	4	0	-2	0	0	-3	-2	-2	-2	-2	0	-2
P	0	0	4	2	5	14	-2	0	91	1	2	-2	-3	-2	4
Q	-4	3	-3	-3	-1	-3	-1	0	-4	7	-3	-1	2	-1	-1
R	-4	-5	2	-8	1	-4	-2	0	-8	2	9	3	9	-2	2
S	4	-2	-5	11	-6	4	9	71	-12	-5	4	8	-1	-2	-5
T	2	1	4	2	4	4	1	29	-5	6	-1	-1	-4	1	8
V	-1	5	1	-1	-4	4	-2	0	-5	1	-2	1	1	-1	4
W	0	-1	-1	-1	0	-1	-1	0	-1	-1	-1	0	-1	-1	2
Y	-1	-1	-1	-2	-2	2	-1	0	-2	-1	1	-2	-1	-1	-2

Table 3. Percent amino acid frequency from random surrounding 70 CDK5 phosphorylation sites.

Substrate Protein	Phospho-Site	Kinex %CFC	Phospho-Site Sequence	Novelty	(+1P)
Adducin α	S726	35	KKKFRTPSFLKKSKK	N	F
AMPKα1/2	T174/T172	179	SDGEFLRTSCGSPNY	N	F
Caveolin 2	S23	96	DDSYSHHSGLEYADP	N	F
Caveolin 2	S36	38	DPEKFADSDQDRDPH	N	F
CREB1	S129+S133	26	QKRREILSRRPSYRK	N	F
eIF2Bε	S540	25	MDSEEPDSRGGSPQM	N	F
GAP-43	S41	227	AATKIQASFRGHITR	N	F
Histone H3	S28	68	ATKAARKSAPATGGV	N	F
Hsp27	S86	33	RQLSSGVSEIRHTAD	N	F
Hsp27	S78	25	PAYSRALSRQLSSGV	N	F
MLK3	T277+S281	43	LAREWHKTTQMSAAG	N	F
Msk1	S376	95	EKLFQGYSFVAPSIL	N	F
p53	S392	36	FKTEGPDSD_____	N	F
PDK1	S244 (S241)	29	SKQARANSFVGTAQY	N	F
PKA Cβ	S338	29	EEEEIRVSINEKCGK	N	F
PKCε	S729	35	QEEFKGFSYFGEDLM	N	F
PKCθ	T538	145	LGDAKTNTFCGTPDY	N	F
Raf1	S259	30	SQRQRSTSTPNVHMV	N	F
S6Kα (p70/p85 S6Kα)	T389	55	NQVFLGFTYVAPSVL	N	F
SHP2	S576	30	CAEMREDSARVYENV	N	F
Smad1/5/9	S463+S465/S463+S465/S465+S467	34	GSPHNPISSVS____	N	F
Smad2	S465+S467	25	SPSVRCSSMS_____	N	F
Synapsin 1	S603	174	AGPTRQASQAGPVPR	N	F
Synapsin 1	S9	59	NYLRRRLSDSNFMAN	N	F
Tyrosine Hydroxylase	S71	106	RFIGRRQSLIEDARK	N	F
ATF2	T53	57	IVADQTPTPTRFLKN	C	T
FAK	S910	29	KLQPQEISPPPTANL	C	T
Jun	S63	58	KNSDLLTSPDVGLLK	C	T
MAPKAPK2α	T334	80	QSTKVPQTPLHTSRV	C	T
MEK1 (MAP2K1)	T291	48	ETPPRPRTPGRPLSS	C	T
RSK1/2	S380/S386	134	HQLFRGFSFVATGLM	C	F
RSK1/2	S363/S369	45	TSRTPKDSPGIPPSA	C	T
RSK1/3	T359+S363/T356+S360	68	DTEFTSRTPKDSPGI	C	T
S6Kα (p70/p85 S6Kα)	T421+S424	46	RFIGSPRTPVSPVKF	C	T
Tau	S202	26	SGYSSPGSPGTPGSR	C	T
Crystallin αB	S45	27	FSTATSLSPFYLRPP	N	T
MEK2 (MAP2K2)	T394	71	LRLNQPGTPTRTAV_	N	T
Rb	S608	45	TAADMYLSPVRSPKK	N	T
Rb	S612	40	MYLSPVRSPKKKGST	N	T
Rb	S780	34	STRPPTLSPIPHIPR	N	T
Tau	S515+S518	25	GDRSGYSSPGSPGTP	N	T

Table 4. Candidate phospho-sites for phosphorylation by ERK2 detected with Kinex™ KAM-1.1 microarray.

Table 4 on the previous page provides a listing of putative substrates for ERK2 in the HeLa cell lysates that were identified from the Kinex™ KAM-1.1 antibody microarray and identified as corresponding to serine or threonine phosphorylation sites. Strong and moderate positive determinants for ERK2 recognition are coloured in blue and orange, respectively, in the "Phospho-site Sequence". Out of the 41 sequences shown, 26 did not feature a proline residue at the +1 position (indicated with an "F" in the last column marked "(+1P)" in Table 4). Out of 250 known ERK2 phosphorylation sites in substrate proteins reported in the scientific literature, the 14 shown in Table 5 below also do not have a proline residue at the +1 position. Therefore, it is possible that some of the putative phospho-sites in Table 4 that are missing a proline at the +1 position are substrates of ERK2. However, for most of these phospho-site antibodies, it is likely that cross-reactive phosphoproteins were detected rather than the intended targets. These could be followed up by immunoprecipitation and MALDI mass spectrometry identification.

Substrate Protein	Phospho-Site	Phospho-Site Sequence
Akt1 (mouse)	T308	**KDGATMKTFCGTPEY**
ATP1A1 (rat)	S16	**KYEPAAVSEHGDKKS**
Calpain 2 (human)	S49	**GTLFQDPSFPAIPSA**
Crystallin alphaB (human)	S59	**PSFLRAPSWIDTGLS**
GATA-1 (human)	S26	**VDPALVSSTPESGVF**
KSR1 (human)	S443	**AMNHLDSSSNPSSTT**
p53 (human)	S15	**PSVEPPLSQETFSDL**
p53 (mouse)	S18	**ISLELPLSQETFSGL**
Paxillin (human)	S83	**FIHQQPQSSSPVYGS**
RSK2 (mouse)	S386	**HQLFRGFSFVAITSD**
SOS1 (human)	S1132	**TLPHGPRSASVSSIS**
SOS1 (human)	S1197	**KAYSPRYSISDRTSI**
Spinophilin (mouse)	S15	**GPGGPLRSASPHRSA**
TR-beta1 (human)	S142	**IQKNLHPSYSCKYEG**

Table 5. Known Erk2 phosphorylation sites that do not feature a proline residue at the +1 amino acid position.

The remaining 15 phospho-sites shown in Table 4 exhibited a proline residue at the +1 amino acid position (indicated with a "T"). Of these, 9 have previously reported to be substrates of ERK2 (indicated with a "C" for "confirmed" in the "Novelty" column in Table 4). The other 6 phospho-sites (indicated with a "N" for "novel") have not been previously reported, and all of them feature multiple positive determinants for ERK2 recognition. Figure 2 shows the immunoblotting results that were obtain when some of the identified phospho-site antibodies were tested for their ability to detect increased ERK2 phosphorylation of the target proteins. These findings confirm the ability of the Kinex™ KAM-1.1 microarray to uncover known and novel detection phospho-site antibodies for kinase substrates.

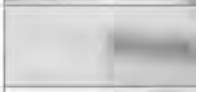
Substrate Protein	Phospho-Site	Kinex %CFC	Western Blot
MAPKAPK2α	T334	80	
MEK1 (MAP2K1)	T291	48	
MEK2 (MAP2K2)	T394	71	
RSK1/3	T359+S363/ T356+S360	68	
RSK1/2	S380/S386	134	
S6Kα p70/p85	T421+S424	46	

Figure 2. Examples of ERK2 substrates in HeLa cell lysates detected with phospho-site-specific antibodies. Detected bands correspond to the expected sizes of the target phosphoproteins. %CFC refers to the percent increased phosphorylation of the target protein by the added ERK2 as detected with the Kinex™ KAM-1.1 antibody microarray. With the Western blots, minus ERK2 is on the left and plus ERK2 is on the right.

Like ERK2, CDK5 is known to be a proline-directed kinase, such that all of its reported substrates feature a proline residue at the +1 amino acid position. Table 6 provides a listing of 19 putative phosphorylation sites in substrates for CDK5 in the HeLa cell lysates that were identified from the Kinex™ KAM-1.1 antibody microarray and found to possess a serine or threonine phosphorylation site with a proline at the +1 position. Strong and moderate positive determinants for CDK5 recognition are coloured in blue and orange, respectively, in the “Phospho-site Sequence”. In Figure 3, Kinex™ KAM-1.1 microarray and subsequent immunoblotting results are provided for the some of the serine and threonine phospho-site-specific antibodies that shown enhanced phosphorylation of proteins with the addition of CDK5, regardless of whether or not they featured a proline residue at the +1 amino acid position. Histone H1 is commonly used as a substrate to monitor CDK5 phosphotransferase activity. It is evident in Figure 3 that several of the other phospho-site antibodies (e.g. for phospho-Rb) identified from the CKSP Service are much better probes of CDK5 activity that phospho-Histone H1. Interestingly, Protein Kinase C-mu (PKD) S738 was identified as a strong candidate for CDK5 phosphorylation by immunoblotting, even though a proline residue is not located at the +1 position. This phospho-site does contain at least 3 other positive determinants for CDK5 phosphorylation, and PKC-mu does not feature any other suitable CDK5 sites with a proline at the +1 position and shared amino acids with the target sequence for the PKC-mu phospho-S738 antibody. Another intriguing possible CDK5 substrate is the receptor protein-tyrosine kinase Ret at its T1022 site. This site features several positive determinants for recognition by CDK5 and it is reasonable that it might be recognized by the Ret phospho-S696 antibody. Both Ret sequences feature phosphorylated residues at the 0 amino acid position, neighbouring Asp-Ser on the C-terminal side of these sites. This strategy of considering both the antigenic sequence of the original phospho-site target of the detecting phospho-antibody and the substrate consensus recognition sequence of a protein kinase improves the prospects for successful identification of physiological substrates of this kinase.

Protein	Phospho-Site	Phospho-Site Sequence	Kinex %CFC
Arrestin β1	S412	EEEDGTGSPQLNNRX	25
Crystallin αB	S19	RPFFPFHSPSRLFDQ	45
Crystallin αB	S45	FSTATSLSPFYLRPP	40
Fos	T232	GGLPEVATPESEEAF	28
MEK1 (MAP2K1)	T385	IGLNQPSTPTHAAGV	63
MEK2 (MAP2K2)	T394	LRLNQPGTPTRTAVX	43
Pax2	S394	SNPALLSSPYYYSAA	99
PKCγ	T655	TRAAPALTPPDRLVL	28
PKCλ/ι	T555	TNEPVQLTPDDDDIV	74
Rb	S608	TAADMYLSPVRSPKK	83
Rb	S612	MYLSPVRSPKKKGST	28
Rb	S807	PGGNIYISPLKSPYK	112
Rb	T826	LPTPTKMTPRSRILV	35
RSK1/2	T573/T577	AENGLLMTPCYTANF	45
STAT1	S727	TDNLLPMSPEEFDEV	31
STAT3	S727	NTIDLPMSPRTLDSL	38
Tau	S202	SGYSSPGSPGTPGSR	31
Tau	S515+S518	GDRSGYSSPGSPGTP	26
Tau	S712	GAEIVYKSPVVSGDT	34

Table 6. Putative CDK5 phosphorylation sites that feature a proline residue at the +1 amino acid position.

Substrate Protein	Phospho-Site	Phospho-Site Sequence	Kinex %CFC
Crystallin αB	S19	RPFFPFHSPSRLFDQ	45
Histone H1	T135+T153+T199	ATPKK	50
MEK2 (MAP2K2)	T394	LRLNQPGTPTRTAVX	43
PKCλ/ι	T555	TNEPVQLTPDDDDIV	74
PKCμ (PKD)	S738+S742	ARIIGEKSFRRSVVG	71
Rb	S608	TAADMYLSPVRSPKK	83
Rb	T826	LPTPTKMTPRSRILV	35
RSK1/2	T573/T577	AENGLLMTPCYTANF	45
Ret	S696 T1022	SSGARRPSLDSMENQ YLDLAASTPSDSLIY	155

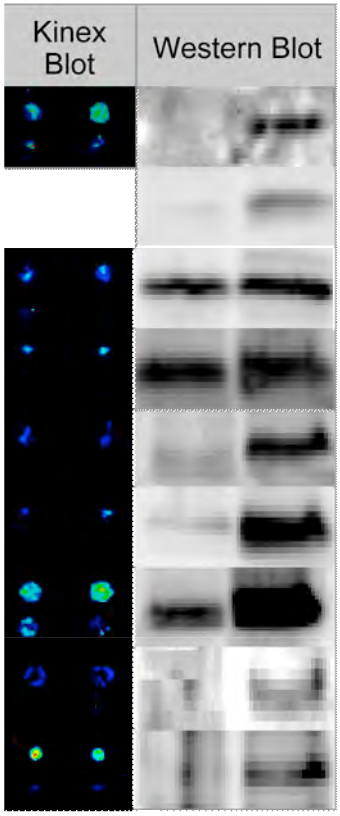


Figure 3. Immunoblotting analysis of putative CDK5 phosphorylation sites. The column with the "Kinex Blot" shows the section of the Kinex™ KAM-1.1 microarray with the scanned image of the pairs of spots corresponding to the tested phospho-site antibody. Antibody spots incubated with lysates treated with CDK5 and ATP are the upper pair, whereas the lower pair arises lysates incubated with ATP from the absence of added CDK5. With the Western blots, minus CDK5 is on the left and plus CDK5 is on the right.

A large body of information and instruction follows in this customer information package. Your careful review of this package will ensure that we can provide to you the highest level of quality with our unique proteomics services. Eventually, we do plan to share the results of our Custom Kinase Substrate Profiling analyses with other scientists in our KiNET DataBank and SigNET Knowledgebank. For these rights, we have discounted our standard charges by 40% with our Non-Confidential Pricing option. The data available in KiNET and SigNET should prove to be very useful for your own reference at a later date when you compare it with your own findings using our proteomics services. Should you have any questions or concerns, we would be pleased to hear from you. Thank you in advance for letting Kinexus become one of your trusted research partners.

4. CLIENT SUPPLIED CELL AND TISSUE LYSATES

The minimum amount of cell or tissue lysate protein required for the Custom Kinase Substrate Profiling Service is 1000 μg per sample at a minimum concentration of 2 mg/ml (please adjust concentration accordingly with lysis buffer). The samples must be frozen and shipped to Kinexus on dry ice fresh after protein quantification **WITHOUT ANY SDS-PAGE SAMPLE BUFFER** as the proteins are to remain in their native structure and nondenatured for the Kinex™ antibody microarray analysis. The cell pellet or tissue should be homogenized in the following ice-cold lysis buffer and the final pH of the lysis buffer should be adjusted to 7.2.

1. 20 mM MOPS, pH 7.0 (any other buffer without Tris at this pH could be substituted);
2. 20 mM sodium fluoride (to inhibit protein-serine phosphatases);
3. 60 mM β-glycerophosphate, pH 7.2 (to inhibit protein-serine phosphatases);
4. 20 mM sodium pyrophosphate (to inhibit protein-serine phosphatases);
5. 1 mM sodium orthovanadate (to inhibit protein-tyrosine phosphatases);
6. 1 mM phenylmethylsulfonylfluoride (to inhibit proteases);
7. 3 mM benzamidine (to inhibit proteases);
8. 5 μM pepstatin A (to inhibit proteases);
9. 10 μM leupeptin (to inhibit proteases);
10. 1% Triton X-100 (can be substituted with 1% Nonidet P-40)
    Important Note: *Do not add if you intend to first prepare a cytosolic fraction;*
11. 1 mM dithiothreitol (to disrupt disulphate bonds).
    Important Note: *dithiothreitol must be added to lysis buffer immediately before use.*

NOTE: Other lysis buffers commonly used for protein lysate preparation with non-ionic detergents should still be compatible with the service, but any buffers containing Tris or reagents carrying reactive amine groups will NOT be acceptable alternatives. Please contact a Kinexus Technical Sales Representative for more information on the appropriate types of lysis buffers to use for the Kinex™ Antibody Microarray Services or to request to have an aliquot of our lysis buffer for free if you can provide a courier account number to charge for the shipping costs. Our lysis buffer contains components 1-5, including phosphatase inhibitors (components 2-5) but *no protease inhibitors and dithiothreitol* (components 7-11). Clients must add their own dithiothreitol and protease inhibitors to the lysis

buffer immediately before use. For convenience, they may choose to use the Roche Complete, Mini inhibitor cocktail tablet with the addition of pepstatin A as opposed to individual protease inhibitors.

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

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

Other fractionation: We do not recommend that you send samples from immunoprecipitation or antibody affinity pull-down experiments for the Custom Kinase Substrate Profiling Service.

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

5. CELL LYSATE PREPARATION

A. Adherent Cell Lysates

1. Remove medium from culture dishes containing about 1×10^7 to 2×10^7 cells;
2. Rinse the cells twice with ice-cold PBS to remove medium residue (serum must be completely removed from cells); remove as much PBS as possible after the last rinse;
3. Add 200 μl ice-cold lysis buffer to 150 mm culture dish per sample (more lysis buffer can be added if cells are concentrated); (add 100 μl ice-cold lysis buffer to 100 mm culture dish)
4. Scrape the cells in lysis buffer, collect the cell suspension from the dishes and transfer it into a 1.5-ml microcentrifuge tube;
5. Sonicate four times for 10 seconds each time with 10-15 second intervals on ice to rupture the cells and to shear nuclear DNA; **this step is crucial and cannot be omitted**;
6. Centrifuge the homogenate at 90,000 x g or higher for 30 min at 4°C in a Beckman Table Top TL-100 ultracentrifuge, Beckman Airfuge or equivalent;
7. Transfer the resulting supernatant fraction to a 1.5-ml microcentrifuge tube;
8. Assay sample for protein concentration using a commercial Bradford assay reagent (available from Bio-Rad, catalogue number 500-0201) or using the standard protocol of Bradford *(Bradford, M.M. (1976) A rapid and sensitive method for quantitation of microgram quantities of protein utilizing the principle of protein-dye binding. Anal. Biochem. 72:248-254)*. Bovine serum albumin should be used as the protein standard.

B. Suspended Cell Lysates

1. Place medium containing cells in appropriate sized tube and centrifuge at 500 x g for 2 minutes at 4°C in a swinging bucket benchtop centrifuge. Remove as much medium from the cell pellet as possible without disrupting cells;
2. Wash the pellet by gently resuspending the cells in ice-cold PBS, followed by centrifugation as above. Repeat once to ensure complete removal of serum;
3. Remove as much PBS as possible after the last wash;
4. Add an adequate amount of ice-cold lysis buffer to the sample (more lysis buffer can be added if the number of cells is high);
5. Sonicate four times for 10 seconds each time with 10-15 second intervals on ice to rupture the cells and to shear nuclear DNA; **this step is crucial and cannot be omitted**;
6. Centrifuge the homogenate at 90,000 x g or higher for 30 min at 4°C in a Beckman Table Top TL-100 ultracentrifuge, Beckman Airfuge or equivalent;
7. Transfer the resulting supernatant fraction to a 1.5-ml microcentrifuge tube;
8. Assay sample for protein concentration using a commercial Bradford assay (available from Bio-Rad, catalogue number 500-0201) or using the standard protocol of Bradford *(Bradford, M.M. (1976) A rapid and sensitive method for quantification of microgram quantities of protein utilizing the principle of protein-dye binding Anal. Biochem. 72:248-254).* Bovine serum albumin should be used as the protein standard.

6. TISSUE LYSATE PREPARATION

1. Use 1 ml of lysis buffer per 250 mg wet weight of the chopped tissue;
2. Rinse the tissue pieces in ice-cold PBS three times to remove blood contaminants;
3. Homogenize the tissue on ice with 15 strokes of a glass dounce (or 3 times for 15 seconds each time with a Brinkman Polytron Homogenizer or with a French Press as alternatives);
4. Sonciate the homogenate 4 times for 10 seconds on ice each time to shear nuclear DNA;
5. Centrifuge the homogenate at 90,000 x g or higher for 30 min at 4°C in a Beckman Table Top TL-100 ultracentrifuge, Beckman Airfuge or equivalent;
6. Transfer the resulting supernatant fraction to a new tube and subject it to protein assay. Using a commercial Bradford assay (available from Bio-Rad, catalogue number 500-0201) or using the standard protocol of Bradford *(Bradford, M.M. (1976) A rapid and sensitive method for quantitation of microgram quantities of protein utilizing the principle of protein-dye binding Anal. Biochem. 72:248-254).* Bovine serum albumin should be used as the protein standard.

7. PREPARATION FOR STORAGE AND SHIPPING OF LYSATE AND KINASES SAMPLES

The final protein concentration of the cell/tissue samples should be **a minimum of 2 mg/ml**. If you are unable to achieve that concentration, please contact a customer service representative for assistance and suggestions. Please record the actual concentration and volume of each sample on the Sample Description Form (CKSP-NSDF-01 or CKSP-CSDF-01). Kinexus requests **1000 µg** of cell or tissue lysate for each sample submitted for analysis with the Custom Kinase Substrate Profiling Service. Samples should be stored in *screw cap* vials. The vials should be clearly labeled with an indelible marker with a unique identification number (recorded in the Sample Description

Form), parafilmed, and then put into another support structure such as a 50-ml conical or centrifuge tube to provide extra protection during shipping. **All lysate samples *must* be shipped on dry ice.**

With our Custom Kinase Substrate Profiling Service, many cell lysates and a wide selection of purified and active protein kinases are available as part of this very convenient and cost effective service package. However, we do provide the option for our clients to submit their own protein kinases for use in this analysis in addition to those offered by Kinexus. In this event, clients should complete the Client Supplied Non-Confidential Kinase Description Form (CKSP-NKDF-01) provided in this client information package. If you do not wish to provide the requested information, then a Client Supplied Confidential Kinase Description Form (CKSP-CKDF-01) must be completed, and full confidential pricing charges will be applied. We recognize that not all of the requested information about commercial protein kinases may be available to our clients, so please provide as much information as you are able to qualify for non-confidential pricing.

We recommend that the client supplied protein kinases are provided as concentrated as possible, preferably at around 10.1 mg/ml and within *screw cap* vials. We need approximately 10 µg of most protein kinases. As there are large variations in the phosphotransferase activity of protein kinases, and every kinase is unique, and we may be able to perform the Custom Kinase Substrate Profiling Service with less kinase if it still works well at a lower concentration. The vials should be clearly labeled with an indelible marker with a unique identification number (recorded in the CKSP-NKDF-01 or CKSP-CKDF-01 forms), parafilmed, and then put into another support structure such as a 50-ml conical or centrifuge tube to provide extra protection during shipping. **All kinase samples *must* be shipped on dry ice.**

8. SHIPPING INFORMATION

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

Kinexus Bioinformatics Corporation
Suite 1, 8755 Ash Street
Vancouver, B.C. Canada V6P 6T3
Telephone: (604) 323-2547
Facsimile: (604) 323-2548
E-mail: info@kinexus.ca

Please ensure 3 copies of a signed commercial invoice (available near the end of this customer information package) accompany your shipment which specifies your lysate and kinase samples are non hazardous and non infectious. Since the protein samples are not for resale, the value of your shipment should be priced at approximately $1.00 per sample in order to avoid paying additional duties and taxes on entry into Canada. It is highly recommended that customers e-mail their courier airway bill number and the date of departure to info@kinexus.ca so we can track your shipment in transit and ensure it arrives in a timely manner. We will send a confirmation e-mail once your shipment arrives at our facility.

9. PRICING INFORMATION

Kinexus offers the Custom Kinase Substrate Profiling Service at two different pricing levels depending on the level of confidentiality required. Our regular prices for the CKSP service starts at US $4496 for each kinase and lysate pair selected for analysis if sample information is to remain fully confidential. At this pricing level, if the client provides their own lysate and/or protein kinase, only partial information about these preparations need to be disclosed in the CKSP-CSDF-01 or CKSP-CKDF-01 forms. To receive a 40% discount off the regular price, or pay US $2296 for each kinase and lysate pair, Kinexus must be allowed after at least a 6 month hold to include the results in its on-line KiNET DataBank and SigNET KnowledgeBank, which will permit third parties to access the data. If the client supplies their own cell/tissue lysates and/or protein kinases for probing the microarray, then they must also complete in full a CKSP-NSDF-01 form and/or a CKSP-CKDF-01 form.

For volume discounts or quotations for large orders, please contact the Director of Sales & Marketing at 1-866-KINEXUS (or 1-604-323-2547) (and select option 2 on the telephone directory) or e-mail sales@kinexus.ca.

10. FOLLOW UP SERVICES

Kinexus offers several services to cost-effectively follow up the results from our Custom Kinase Substrate Profiling Service. Clients can utilize our Kinetworks™ Custom KCSS 1.0 (Multi-Sample) Protein Screen for analysis of 8 different cell or tissue lysates and choose up to 3 different phospho-site antibodies (provided the molecular weights are significantly separated by SDS-PAGE). Clients can correlate their phospho-site results with hundreds of other measurements of protein phosphorylation in hundreds of different model systems using our KiNET Database. Clients can also investigate the regulation of specific phospho-sites in hundreds of cell and tissue lysates with our Kinex™ Reverse Lysate Microarray Service. With our IHC Immunohistochemistry Service, we can track the location of phosphorylation changes in tissue sections. For presentation and publication purposes with the results from this Custom Kinase Substrate Profiling Service, we can prepare figures and tables with our Custom Graphics Services. For more information about these services, please contact one of our customer service representatives at info@kinexus.ca.

11. FORMS TO BE COMPLETED

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

A. Kinexus Service Agreement. Customers are required to complete and sign our standard Kinexus Services Agreement before their first order can be processed. Unless otherwise specified, this Agreement is valid for all future orders with a standard term of 15 years.

B. Service Order Form (CKSP-SOF-01). The Service Order Form (SOF) allows us to track all of the various services to be used within an order.

C. Service Identification Form (CKSP-SIF-01). The Service Identification Form (SIF) permits us to determine which Kinexus or client-supplied cell/tissue lysates and protein kinases are to be used for the Custom Kinase Substrate Profiling Service.

If customers wish to send their own cell or tissue lysates or purified protein kinases, they must also complete and submit the following forms:

D. Client Supplied Non-Confidential Sample Description Form (CKSP-NSDF-01). Completion of this form is necessary for qualification for the Non-Confidential pricing discount.
E. Client Supplied Confidential Sample Description Form (CKSP-CSDF-01). Completion of this form is necessary if the customer wishes to use the fully confidential service.
F. Client Supplied Non-Confidential Kinase Description Form (CKSP-NKDF-01). Completion of this form is necessary for qualification for the Non-Confidential pricing discount.
G. Client Supplied Confidential Kinase Description Form (CKSP-CKDF-01). Completion of this form is necessary if the customer wishes to use the fully confidential service.
H. Federal Express Airway Bill. For probing antibodies to be delivered by Federal Express. Clients can pick any courier of their choice, but we recommend Federal Express within North America.
I. Commercial Invoice. This is required for all customers located outside of Canada that send cell or tissue lysates or purified protein kinases.

All orders should have as a minimum: 1 SOF and 1 SIF forms completed. A new Kinexus Services Agreement may not be necessary if the client has previously placed an order with Kinexus and submitted a signed Kinexus Services Agreement at that time.

FOR ALL CUSTOMERS

A. Kinexus Service Agreement

A Kinexus Service Agreement is required to be signed before the first order can be processed.

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

B. Service Order Form (CKSP-SOF-01)

Please ensure:

- Shipping address and contact name and numbers are specified.
- Billing information is completed on the Service Identification Form (CKSP-SIF-01).
- Any promotional vouchers or quotations are listed in the billing sections.
- Include a Purchase Order, Visa or MasterCard number for payment.
- The form is signed and dated.

C. Service Identification Form (CKSP-SIF-01)

For each cell/tissue lysate or protein kinase to be used for the analysis, please ensure the following:

- In Section A, the various combinations of cell/tissue lysates with the protein kinases to be used are specified.
- In Section B, the customer must assign a unique Client Identification Name to identify the cell or tissue lysate to be used in the combination with the right protein kinase. The cell or tissue lysate to be used should also be identified by completion of a Client Supplied Sample Description Form, either CKSP-NSDF-01 or CKSP-CSDF-01, depending on the level of confidentiality. If multiple cell/tissue lysates are to be analyzed, enter each of these ID names into Box B on the CKSP-SIF-01 form. Make sure to also include the ID name in Box A in the column under the Lysate Code in this case so that it can be matched with the appropriate added protein kinase.
- For Section C, the customer must assign a unique Client Identification Name to identify the protein kinase supplied by the client to be used in the combination with the right protein kinase. The protein kinase to be used should also be identified by completion of a Client Supplied Kinase Description Form, either CKSP-NKDF-01 or CKSP-CKDF-01, depending on the level of confidentiality. If multiple kinases are to be analyzed, enter each of these ID names into Box C as appropriate on the CKSP-SIF-01 form. Make sure to also include the ID name in Box A in the column under the Kinase Code in this case so that it can be matched with the cell or tissue lysate.
- Make sure that the Client ID Names in Box A of the various appropriate description forms (i.e. CKSP-NSDF-01. CKSP-CSDF-01, CKSP-NKDF-01 or CKSP-CKDF-01) matched the Client ID Names in Boxes B and C of the CKSP-SIF-01 form.
- In Section D, the level of confidentiality is indicated for correct pricing.
- The form is certified correct and signed and dated.

FOR ALL CUSTOMERS SENDING THEIR OWN CELL OR TISSUE LYSATES OR PROTEIN KINASES

D. Client Supplied Cell/Tissue Lysate and Protein Kinase Description Forms (CKSP-NSDF-01, CKSP-CSDF-01, CKSP-NKDF-01, CKSP-CKDF-01)

For submitted cell/tissue lysates and/or protein kinases, please ensure the following:

- Each lysate and/or protein kinase sample tube is labeled and properly identified on the form in Section B, including final concentration and volume.
- In Section A, the customer must enter the unique Client Identification Name from Boxes B and C of the Service Identification Form (CKSP-SIF-01) to match the cell/tissue lysate to the appropriate protein kinase for the Custom Kinase Substrate Profiling Service. If multiple cell/tissue lysates or multiple kinases are to be analyzed, enter each of these ID names into Boxes B and C as appropriate on the CKSP-SIF-01 form.
- The form is certified correct and signed and dated.
- Note that the information provided on this form will eventually become available to thousands of other scientists in the future with the non-confidentiality pricing. In the spirit of collegiality, please be as accurate as possible in completing the CKSP-NSDF-01 and CKSP-NKDF-01 forms in order not to handicap their research efforts should they desire to follow up on your Custom Kinase Substrate Profiling Service Results.

E. Airway bill for Federal Express or any other courier

Complete the airway bill and specify:

- Priority overnight delivery.
- Bill transportation charges to your institute.
- It is not critical to send your antibody in a frozen state. However, if you wish to send your antibody frozen please provide sufficient dry ice to last several days into a Styrofoam shipping container.
  Seal the edges of the Styrofoam container with tape to preserve dry ice longer.
  Dry ice is a "*hazardous"* item, so ensure proper labels are attached to the outside of the box.
- Do not specify Saturday delivery or hold at courier location.
- For Federal Express shipments telephone 1-800-GO-FEDEX or visit them on-line at www.fedex.com or www.fedex.ca to schedule a pick up or complete your forms.
- For shipments coming from within Canada or the United States, please ship any day from Monday to Wednesday. Do not ship on a Thursday or Friday.
- For international shipments coming from outside of North America, the best day to ship is on a Monday to ensure arrival in Canada for delivery later the same week.
- It is recommended that customers e-mail the date of your shipment and the courier airway bill number with number of samples to Kinexus at info@kinexus.ca to ensure we can track your package should it get held up in Canadian Customs.
- For any customer located outside of Canada, 3 copies of a commercial invoice is required to accompany your shipment (see below).

FOR U.S AND INTERNATIONAL CUSTOMER ONLY

F. Commercial Invoice (not required by Canadian customers)

Please complete the attached commercial invoice with the following information:

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

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

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

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

Appendix 1 - List of Active Protein Kinases

This list may change with respect to availability and pricing.

Protein Kinase Name	Code	U.S. Price
Abl1	AB01	$200.00
Abl1 [E255K]	AB02	$400.00
Abl1 [G250E]	AB03	$400.00
Abl1 [H369P]	AB04	$600.00
Abl1 [T315I]	AB05	$400.00
Abl1 [Y253F]	AB06	$400.00
Abl1 [M351T]	AB07	$600.00
Abl1 [Q252H]	AB08	$600.00
Abl2 (Arg)	AB09	$200.00
ACK	AC01	$200.00
ACVR1 (ALK2)	AC02	$400.00
ACVRL1	AC03	$400.00
ADRBK1 (GRK2)	AD01	$200.00
ADRBK2 (GRK3)	AD02	$400.00
Akt1/PKBα	AK01	$200.00
Akt1/PKBα [δPH, S473D]	AK02	$600.00
Akt1/PKBα [δPH]	AK03	$600.00
Akt2/PKBβ	AK04	$200.00
Akt2/PKBβ [δPH, S474D]	AK05	$600.00
Akt3/PKBγ	AK06	$200.00
Akt3/PKBγ [S472D]	AK07	$600.00
ALK1	AL01	$200.00
ALK4 (ACVR1B)	AL02	$200.00
AMPKα1/β1/γ1 (PRKAA1/B1/G1)	AM01	$200.00
AMPKα1/β1/γ2 (PRKAA1/B1/G2)	AM02	$200.00
AMPKα1/β1/γ3 (PRKAA1/B1/G3)	AM03	$200.00
AMPKα1/β2/γ1 (PRKAA1/B2/G1)	AM04	$200.00
AMPKα2/β1/γ1 (PRKAA2/B1/G1)	AM05	$200.00
Ark5	AR01	$600.00
Ask1 (MAP3K5)	AS01	$200.00
Aurora A (AurA, AURKA)	AU01	$200.00
Aurora B (AurB, AURKB, INCENP)	AU02	$200.00
Aurora C (AurC, AURKC)	AU03	$200.00
Axl	AX01	$200.00
BARK1 (ADRBK1)	BA01	$600.00
BARK2 (ADRBK2)	BA02	$600.00
Blk	BL01	$200.00
BMPR1A (ALK3)	BM01	$600.00
BMPR1B (ALK6)	BM02	$600.00
Bmx	BM03	$200.00
B-Raf	BR01	$200.00
B-Raf [δ1-415]	BR02	$600.00
B-Raf [V599E]	BR03	$200.00
Brk (PTK6)	BR04	$200.00
BrSK1 (SAD1)	BR05	$400.00
BrSK2	BR06	$600.00
Btk	BT01	$200.00
Btk [E41K]	BT01	$600.00
Btk [R28H]	BT02	$600.00

Protein Kinase Name	Code	U.S. Price
BUBR1(BUB1B)	BU01	$600.00
CaMK1δ (CAMK1D)	CA03	$200.00
CAMK1γ	CA04	$200.00
CAMK2α (CAMK2B)	CA05	$200.00
CaMK2β (CAMK2B)	CA06	$200.00
CaMK2δ (CAMK2D)	CA07	$400.00
CaMK2γ (CAMK2G)	CA08	$600.00
CAMK3γ	CA09	$200.00
CAMK4	CA10	$200.00
CAMK4 (CaMKIV)	CA11	$400.00
CAMKK1 (CAMKKA)	CA12	$200.00
CAMKK2	CA13	$200.00
CAMKK2 (CaMKK beta)	CA14	$400.00
CDC42 BPA (MRCKA)	CD01	$400.00
CDC42 BPB (MRCKB)	CD02	$400.00
CDC7/ASK	CD03	$600.00
CDK1/cyclin B1	CD04	$400.00
CDK1/CyclinA2	CD05	$200.00
CDK2/cyclin A	CD06	$400.00
CDK2/Cyclin E1	CD07	$600.00
CDK2/CyclinA2	CD08	$200.00
CDK3/Cyclin E1	CD09	$600.00
CDK4//Cyclin D3	CD10	$600.00
CDK4/Cyclin D1	CD11	$200.00
CDK5	CD12	$600.00
CDK5/p25	CD13	$200.00
CDK5/p35	CD14	$400.00
CDK6//Cyclin D3	CD15	$600.00
CDK6/cyclin D1	CD16	$400.00
CDK7/Cyclin H1/MAT1	CD17	$200.00
CDK8/Cyclin C	CD18	$400.00
CDK9/Cyclin K	CD19	$200.00
CDK9/Cyclin T1	CD20	$400.00
CGK2 (PRKG2)	CG01	$600.00
CHK1 (CHEK1)	CH01	$200.00
CHK2 (CHEK2)	CH02	$200.00
CK1α (CSNK1A1)	CK01	$400.00
CK1δ (CSNK1D)	CK02	$400.00
CK1δ (CSNK1D) [1-294]	CK03	$600.00
CK1ε (CSNK1E)	CK04	$400.00
CK1γ1 (CSNK1G1)	CK05	$400.00
CK1γ2 (CSNK1G2)	CK06	$400.00
CK1γ3 (CSNK1G3)	CK07	$400.00
CK1γ3 (CSNK1G3)	CK08	$400.00
CK2α1 (CSNK2A1)	CK09	$200.00
CK2α2 (CSNK2A2)	CK10	$400.00
CLK1	CL01	$200.00
CLK2	CL02	$200.00
CLK3	CL03	$400.00

Appendix 1 - List of Active Protein Kinases (Cont'd) - 2

Protein Kinase Name	Code	U.S. Price
CLK4	CL04	$400.00
COT (MAP3K8)	CO01	$200.00
CRIK	CR01	$600.00
Csk	CS02	$200.00
C-TAK1	CT01	$600.00
CTK	CT02	$600.00
DAPK1	DA01	$200.00
DAPK2	DA02	$400.00
DAPK3 (ZIPK)	DA03	$200.00
DCAMKL1	DC01	$600.00
DCAMKL2 (DCK2)	DC02	$400.00
DDR1	DD01	$600.00
DDR2	DD02	$200.00
DLK (MAP3K12)	DL01	$600.00
DMPK1 (DMPK)	DM01	$400.00
DRAK1 (STK17A)	DR01	$600.00
DYRK1A	DY01	$400.00
DYRK1B	DY02	$400.00
DYRK2	DY03	$600.00
DYRK3	DY04	$400.00
DYRK4	DY05	$400.00
eEF2K	EE01	$400.00
EGFR (ErbB1)	EG01	$400.00
EGFR (ErbB1) [L858R]	EG02	$400.00
EGFR (ErbB1) [L861Q]	EG03	$400.00
EGFR (ErbB1) [T790M, L858R]	EG04	$400.00
EGFR (ErbB1) [T790M]	EG05	$400.00
EIF2AK3 (PERK)	EI06	$400.00
EphA1	EP01	$200.00
EphA2	EP02	$400.00
EphA3	EP03	$400.00
EphA4	EP04	$400.00
EphA5	EP05	$400.00
EphA6	EP06	$600.00
EphA7	EP07	$600.00
EphA8	EP08	$600.00
EphA8	EP09	$400.00
EphB1	EP10	$600.00
EphB2	EP11	$400.00
EphB3	EP12	$200.00
EphB4	EP13	$200.00
ErbB2 (HER2, Neu)	ER01	$200.00
ErbB4 (HER4)	ER02	$400.00
Erk1 (MAPK3)	ER03	$600.00
Erk2 (MAPK1)	ER04	$600.00
Erk5 (MAPK7)	ER05	$200.00
FAK (PTK2)	FA01	$400.00
Fer	FE01	$200.00
Fes (Fps)	FE02	$200.00
FGFR1 (FLT2)	FG01	$200.00
FGFR1 (FLT2) [V561M]	FG02	$200.00
FGFR2	FG03	$400.00
FGFR2 [N549H]	FG04	$600.00
FGFR3	FG05	$200.00
FGFR3 [K650E]	FG06	$400.00
FGFR3 [K650M]	FG07	$600.00

Protein Kinase Name	Code	U.S. Price
FGFR4	FG08	$200.00
Fgr	FG09	$600.00
Flt1 (VEGFR1)	FL01	$400.00
Flt3	FL02	$200.00
Flt3 [D835Y]	FL03	$400.00
Flt4 (VEGFR3)	FL04	$200.00
Fms (CSF1R)	FM01	$400.00
FRAP1 (mTOR)	FR01	$600.00
FRK (PTK5)	FR02	$400.00
Fyn	FY01	$200.00
GRK4	GR01	$400.00
GRK5	GR02	$200.00
GRK6	GR03	$400.00
GRK7	GR04	$600.00
GSK3α	GS01	$200.00
GSK3β	GS02	$400.00
Haspin (GSG2)	HA01	$200.00
Hck	HC01	$200.00
Hgk (MAP4K4)	HG01	$400.00
HIPK1 (Myak)	HI01	$200.00
HIPK2	HI02	$200.00
HIPK3	HI03	$200.00
HIPK3 (YAK1)	HI04	$200.00
HIPK4	HI05	$600.00
IGF1R	IG01	$400.00
IGF1R [δ1-958]	IG02	$600.00
IKKα (CHUK)	IK01	$200.00
IKKβ (IKBKB)	IK02	$200.00
IKKε (IKBKE)	IK03	$400.00
INSRR (IRR)	IN01	$200.00
Insulin Rec. (INSR)	IN02	$400.00
IRAK1	IR01	$600.00
IRAK2	IR02	$200.00
IRAK4	IR03	$400.00
Itk	IT01	$200.00
JAK1	JA01	$600.00
JAK2	JA02	$200.00
JAK2 [JH1, JH2, V617F]	JA03	$600.00
JAK2 [JH1, JH2]	JA04	$400.00
JAK3	JA05	$400.00
JNK1a1 (MAPK8)	JN01	$400.00
JNK2α2 (MAPK9)	JN02	$600.00
JNK3 (MAPK10)	JN03	$600.00
KDR (VEGFR2)	KD01	$400.00
KHS1(MAP4K5)	KH01	$400.00
Kit	KI01	$200.00
Kit [D816H]	KI02	$600.00
Kit [D816V]	KI03	$600.00
Kit [T670I]	KI04	$400.00
Kit [V560G]	KI05	$200.00
Kit [V654A]	KI06	$200.00
Lck	LC01	$200.00
LIMK1	LI01	$200.00
LIMK2	LI02	$400.00
LKB1 (MO25α, STRADα, STK11)	LK01	$600.00
LOK (STK10)	LO01	$600.00

Appendix 1 - List of Active Protein Kinases (Cont'd) - 3

Protein Kinase Name	Code	U.S. Price
LRRK2	LR01	$600.00
LRRK2 [G2019S]	LR02	$400.00
LTK (TYK1)	LT01	$400.00
Lyn A	LY01	$200.00
Lyn B	LY02	$200.00
MKK5 (MEK5, MAP2K5)	MK01	$600.00
MAP3K14 (NIK)	MA01	$600.00
MEKK3 (MAP3K3)	ME01	$200.00
MAP3K4	MA02	$600.00
MAP3K7-MAP3K7IP1 (TAK1-TAB1)	MA03	$400.00
GCK (MAP4K2)	GC01	$400.00
MAP4K4 (HGK)	MA04	$600.00
MAPKAPK2	MA05	$400.00
MAPKAPK3	MA06	$400.00
MAPKAPK5 (PRAK)	MA07	$400.00
MARK1 (MARK)	MA08	$400.00
MARK2	MA09	$400.00
MARK3	MA10	$400.00
MARK4	MA11	$400.00
MATK (HYL)	MA12	$400.00
MEK1 (MKK1, MAP2K1)	ME01	$200.00
MEK1 (MKK1, MAP2K1) [S218E, S222E]	ME02	$200.00
MEK2 (MKK2,MAP2K2)	ME03	$200.00
MEKK2 (MAP3K2)	ME04	$200.00
MEKK3 (MAP3K2)	ME05	$200.00
MELK	ME06	$400.00
MERTK (Mer)	ME07	$200.00
Met	ME08	$400.00
Met [M1250T]	ME09	$200.00
Met [Y1235D]	ME10	$400.00
MGC42105	MG01	$200.00
MINK1 (MINK)	MI01	$200.00
MKK3 (MEK3, MAP2K3)	MK01	$200.00
MKK4 (MEK4, MAP2K4)	MK02	$400.00
MKK6 (MEK6, MAP2K6)	MK03	$200.00
MKK6 (MEK6, MAP2K6) [S599D, T603D]	MK04	$600.00
MKK7α1 (MEK7α1, MAP2K7A1)	MK05	$400.00
MKK7β1 (MKK7β1, MAP2K7B1)	MK06	$600.00
MLCK (MLCK2, MYLK)	ML01	$200.00
MLK1 (MAP3K9)	ML02	$200.00
MLK2 (MAP3K10)	ML03	$200.00
MLK3 (MAP3K11)	ML04	$200.00
MNK1 (MKNK1)	MN01	$600.00
MNK2 (MKNK2)	MN02	$600.00
MOS	MO01	$600.00
MRCKα (CDC42BPA)	MR01	$600.00
MRCKβ (CDC42BPB)	MR02	$200.00
MSK1 (RPS6KA5)	MS01	$600.00
MSK2 (RPS6KA4)	MS02	$600.00
MSSK1 (STK23)	MS03	$200.00
MST1 (STK4)	MS04	$600.00
MST2 (STK3)	MS05	$200.00
MST3 (STK24)	MS06	$600.00
MST4	MS07	$200.00
MUSK	MU01	$200.00
MYLK2 (skMLCK)	MY01	$400.00
MYO3β	MY02	$400.00
MYT1 (PKMYT1)	MY03	$200.00
NDR1 (STK38)	ND01	$200.00
NEK1	NE01	$200.00
NEK11 (FLJ23495)	NE02	$200.00
NEK2	NE03	$200.00
NEK3	NE04	$200.00
NEK4	NE05	$400.00
NEK6	NE06	$200.00
NEK7	NE07	$600.00
NEK9	NE08	$600.00
NLK	NL01	$400.00
NUAK1 (ARK5)	NU01	$400.00
p38α (MAPK14)	MA13	$200.00
p38α (MAPK14) [T106M]	MA14	$400.00
p38β (MAPK11)	MA15	$400.00
p38δ (MAPK13)	MA16	$200.00
p38γ (MAPK12)	MA17	$200.00
p70S6K (RPS6KB1)	RS01	$400.00
p70S6K (RPS6KB1) [T412E]	RS02	$400.00
p70S6Kβ (RPS6KB2)	RS03	$400.00
PAK1/CDC42	PA01	$200.00
PAK2 (PAK65)	PA02	$600.00
PAK3	PA03	$200.00
PAK4	PA04	$200.00
PAK6	PA05	$200.00
PAK7 (KIAA1264, PAK5)	PA06	$600.00
PAR-1Ba/MARK2	PA07	$200.00
PASK	PA08	$400.00
PBK (TOPK)	PB01	$200.00
PCTAIRE1 (PCTK1)	PC01	$400.00
PDGFRα	PD01	$200.00
PDGFRα [550-end, D842V]	PD02	$200.00
PDGFRα [550-end, V561D]	PD03	$400.00
PDGFRα [D842V]	PD04	$200.00
PDGFRα [T674I]	PD05	$600.00
PDGFRα [V561D]	PD06	$400.00
PDGFRβ	PD07	$400.00
PDHK2 (PDK2)	PD08	$600.00
PDHK3 (PDK3)	PD09	$200.00
PDHK4 (PDK4)	PD10	$600.00
PDK1	PD11	$600.00
PEK (EIF2AK3)	PE01	$400.00
PhKγ1 (PHKG1)	PH01	$400.00
PhKγ2 (PHKG2)	PH02	$400.00
Pim1	PI01	$200.00
Pim2	PI02	$600.00
Pim3	PI03	$600.00
PKAcα (PRKACA)	PK01	$600.00
PKAcβ (PRKACB)	PK02	$200.00

Appendix 1 - List of Active Protein Kinases (Cont'd) - 4

Protein Kinase Name	Code	U.S. Price
PKAcγ (PRKACG)	PK03	$600.00
PKCμ (PRKD1)	PK04	$400.00
PKCα (PRKCA)	PK05	$400.00
PKCβ1 (PRKCB1)	PK06	$200.00
PKCβ2 (PRKCB2)	PK07	$200.00
PKCδ (PRKCD)	PK08	$600.00
PKCε (PRKCE)	PK09	$200.00
PKCγ (PRKCG)	PK10	$200.00
PKCη (PRKCH)	PK11	$200.00
PKCι (PRKCI)	PK12	$200.00
PKCλ (PRKCL)	PK13	$200.00
PKCθ (PRKCQ)	PK14	$200.00
PKCζ (PRKCZ)	PK15	$200.00
PKD1 (PRKD1)	PK16	$200.00
PKD2 (PRKD2)	PK17	$200.00
PKD3 (PRKD3, PRKCN)	PK18	$200.00
PKG1α (PRKG1A)	PK19	$200.00
PKG1β (PRKG1B)	PK20	$200.00
PKG2 (PRKG2)	PK21	$600.00
PKN1 (PRK1)	PK22	$600.00
PKN2 (PRK2)	PK23	$200.00
PKR (EIF2AK2)	PK24	$200.00
PLK1	PL01	$200.00
PLK2	PL02	$600.00
PLK3	PL03	$200.00
PLK4	PL04	$400.00
PRKX	PR01	$600.00
PTK2B (FAK2)	PT01	$600.00
PTK5	PT02	$400.00
Pyk2	PY01	$400.00
Raf1 [Y340E, Y341E]	RA01	$400.00
Raf1 (truncated)	RA02	$600.00
Raf1 [Y340D, Y341D]	RA03	$200.00
Ret	RE01	$600.00
Ret [V804L]	RE02	$400.00
Ret [V804M]	RE03	$400.00
Ret [Y791F]	RE04	$600.00
RIPK2	RI01	$200.00
RIPK5	RI02	$400.00
ROCK1 (ROKβ)	RO01	$600.00
ROCK2 (ROKα)	RO02	$200.00
RON (MST1R)	RO03	$200.00
ROR1	RO04	$600.00
ROR2	RO05	$400.00
Ros	RO06	$400.00
Rse	RO07	$200.00
RSK1 (RPS6KA1)	RS04	$400.00
RSK2 (PRS6KA3)	RS05	$200.00
RSK3 (RPS6KA2)	RS06	$200.00
RSK4 (RPS6KA6)	RS07	$200.00
SGK1	SG01	$600.00
SGK1 [δ1-59, S422D]	SG02	$200.00

Protein Kinase Name	Code	U.S. Price
SGK2	SG03	$400.00
SGK3 (SGKL)	SG04	$600.00
SGT220	SG05	$200.00
SGT222-25UG	SG06	$200.00
SIK	SI01	$200.00
skMLCK (MYLK2)	SK01	$400.00
SLK (STK2)	SL01	$200.00
smMLCK (MYLK)	SM01	$600.00
SNF1LK2 (QIK)	SN01	$200.00
SOK	SO01	$200.00
Src	SR01	$200.00
Src [T341M]	SR02	$600.00
SRMS (Srm)	SR03	$600.00
SRPK1	SR04	$600.00
SRPK2	SR05	$600.00
STK16 (PKL12)	ST01	$400.00
STK25 (YSK1)	ST02	$400.00
STK33	ST03	$200.00
Syk	SY01	$600.00
TAO2	TA01	$400.00
TAO3	TA02	$200.00
TAOK1	TA03	$400.00
TAOK2 (TAO1)	TA04	$400.00
TAOK3 (JIK)	TA05	$200.00
TBK1	TB01	$200.00
TEC	TE01	$400.00
TESK1	TE02	$200.00
TGFβR1 (TGFBR1, ALK5)	TG01	$600.00
TGFβR2	TG02	$600.00
Tie2 (Tek)	TI01	$200.00
Tie2 (Tek) [R849W]	TI02	$200.00
Tie2 (Tek) [Y1108F]	TI03	$400.00
Tie2 (Tek) [Y897S]	TI04	$400.00
TLK2	TL01	$400.00
TNK1	TN01	$600.00
TNK2 (ACK)	TN02	$600.00
TrkA (NTRK1)	TR01	$200.00
TrkB (NTRK2)	TR02	$200.00
TrkC (NTRK3)	TR03	$600.00
TSSK1 (STK22D)	TS01	$200.00
TSSK2 (STK22B)	TS02	$200.00
TTBK1	TT01	$600.00
TTK	TT02	$600.00
TXK	TX01	$400.00
TYK2	TY01	$200.00
TYRO3 (RSE)	TY02	$200.00
VRK1	VR01	$600.00
Wee1	WE01	$600.00
WNK1	WN01	$200.00
WNK2	WN02	$600.00
WNK3	WN03	$600.00
WNK4	WN04	$200.00

Appendix 1 - List of Active Protein Kinases (Cont'd) - 5

Protein Kinase Name	Code	U.S. Price
YES1	YE01	$600.00
ZAK	ZA01	$200.00
ZAP70	ZA02	$600.00
ZIPK	ZI01	$600.00

Appendix 2 - List of Cell Lysates

Cell Line	Ref. Code	Organ/Tissue	Name	Gender	Comments
A431	CL01	Skin	Human	Female	Skin epidermoid carcinoma from an 85 year old female [ATCC# CRL-1555]
A549	CL02	Lung	Human	Male	Lung carcinoma from a 58 year old male [ATCC# CCL-185]
Daudi	CL03	Blood B Cell	Human	Male	Burkitt's B cell lymphoma from a 16 year old male [ATCC# CCL-213]
HCT116	CL04	Colon	Human	Male	Colon carcinoma from an adult male [ATCC# CCL-247]
HEK 293	CL05	Kidney	Human	Female	Female fetal kidney cells transformed with adenovirus 5 [ATCC# CRL-1573]
HeLa	CL06	Cervix	Human	Female	Cervix epithelial adenocarcinoma from 31 year old female [ATCC# CCL-2]
HL-60	CL07	Blood	Human	Female	Peripheral blood promyeloblasts from a 36 year old female [ATCC# CCL-240]
HepG2	CL08	Liver	Human	Male	Liver carcinoma from a 15 year old male [ATCC# HB-8065]
HU-VEC	CL09	Umbilical Cord	Human	Female	Umbilical vein endothelial cells from a normal adult female [ATCC# CRL-1730]
Jurkat	CL10	Blood T Cell	Human	Male	T cell leukemia from a 14 year old male [ATCC# TIB-152]
MCF7	CL11	Breast	Human	Female	Breast epithelial adenocarcinoma from a 69 year old female [ATCC# HTB-22]
PC3	CL12	Prostate	Human	Male	Prostate adenocarcinoma from bone of 62 year old male [ATCC# CRL-1435]
T98G	CL13	Brain	Human	Male	Brain glioblastoma from a 61 year old male [ATCC# CRL-1690]
THP1	CL14	Blood Monocyte	Human	Male	Acute monocytic leukemia from peripheral blood of a 1 year old male [ATCC# CRL-1435]

Appendix 3 - List of Phospho-Site Specific Antibodies

The Custom Kinase Substrate Profiling Service utilizes at least 270 different phospho-site-specific antibodies.
Please note that Kinexus reserves the right to add, delete or substitute antibodies from this list without notification depending on antibody performance and availability. However, in general 98% of all antibodies listed below will be utilized in the antibody microarray analysis.

Target Protein	Target Protein Full Name	Phospho-site	Phospho-site	I.D. Code	Ab Reactivity			Actual Mol. Mass	Obsv. Mol.	Link - Protein	Link - Swiss-
		Human	Mouse		Human	Mouse	Rat	Human	Human	Human	Human
4E-BP1	eukaryotic translation initiation factor 4E binding protein 1 (PHAS1)	S65	S64	PN001	T	T	T	13	17+19+23	NP_004086	Q13541
Abl	Abelson proto-oncogene-encoded protein-tyrosine kinase	Y412	Y412	PK001	T	T	T	123	165	NP_005148	P00519
AcCoA carboxylase	Acetyl coenzyme A carboxylase	S80	S79	PN002	T	T	T	265	199	NP_000655	Q13085
Adducin α	Adducin alpha (ADD1)	S726	S724	PN003	T	T	T	81	122	NP_058432	P35611
Adducin γ	Adducin gamma (ADD3)	S693	S693	PN004	T	T	T	79	79	NP_058432	P35611
AMPKα1/2	AMP-activated protein-serine kinase alpha 1/2	T174/T172	T315	PK002	T	T	T	63 / 62	59	NP_006242	Q13131
Arrestin β1	Arrestin beta 1	S412	none	PN005	T	T	T	47	45	NP_004032	P49407
ATF2	Activating transcription factor 2 (CRE-BP1)	T51+T53	T51+T53	PN006-1	T	T	T	52	54	NP_001871	P15336
ATF2	Activating transcription factor 2 (CRE-BP1)	T51+T53	T51+T53	PN006-2	T	T	T	52	54	NP_001871	P15336
ATM	Ataxia telangiectasia mutated	S1981	S1987	PK115	T	T	T	350	350	NP_000042.3	Q13315
B23 (NPM)	B23 (nucleophosmin, numatrin, nucleolar protein NO38)	T199	T198	PN008	T	T	T	33	38	NP_002511	P06748
B23 (NPM)	B23 (nucleophosmin, numatrin, nucleolar protein NO38)	T234+T237	T232	PN009	T	T	T	33	38	NP_002511	P06748
B23 (NPM)	B23 (nucleophosmin, numatrin, nucleolar protein NO38)	S4	S4	PN007	T	T	T	33	34	NP_002511	
Bad	Bcl2-antagonist of cell death protein	S75	S112	PN010	T	T	T	18	19	NP_004313	Q92934
Bad	Bcl2-antagonist of cell death protein	S91	S128	PN011	T	T	T	18	19	NP_004313	Q92934
Bad	Bcl2-antagonist of cell death protein	S99	S136	PN012	T	T	T	18	31	NP_004313	Q92934
BLNK	B-cell linker protein	Y84	Y84	PN013	T	T	T	50	53+61	NP_037446	O75498
BMX (Etk)	Bone marrow X protein-tyrosine kinase	Y40	Y40	PK003	T	T	T	78	70	NP_001712	P51813
BRCA1	Breast cancer type 1 susceptibility protein	S1497	S1454	PN014	T	T	T	108	174	NP_009225	P38398
Btk	Bruton's agammaglobulinemia tyrosine kinase	Y223	Y223	PK004	T	T	T	76	71	NP_000052	Q06187
Caldesmon	Caldesmon	S789	S526	PN015	T	T	T	93	141 + 108	NP_004333	Q05682
CaMK2α	Calcium/calmodulin-dep. protein-serine kinase 2 alpha	T286	T286	PK005-1	T	T	T	54	45	NP_741960	Q9UQM7
CaMK2α	Calcium/calmodulin-dep. protein-serine kinase 2 alpha	T286	T286	PK005-2	T	T	T	54	45	NP_741960	Q9UQM7
Catenin β	Catenin (cadherin-associated protein) beta 1	S45	S45	PN016	T	T	T	85	84	NP_001895	P35222
Caveolin 2	Caveolin 2	S23	S23	PN017	T	T	T	18	18	NP_001224	P51636
Caveolin 2	Caveolin 2	S36	S36	PN018	T	T	T	18	18	NP_001224	P51636
CDK1/2	Cyclin-dependent protein-serine kinase 1/2	T14+Y15	T14+Y15	PK006	T	T	T	34	28	NP_001777	P06493
CDK1/2	Cyclin-dependent protein-serine kinase 1/2	T161/T160	T161/T160	PK008	T	T	T	34	27	NP_001777	P06493
CDK1/2	Cyclin-dependent protein-serine kinase 1/2	Y15	Y15	PK007-1	T	T	T	34	27	NP_001777	P06493
CDK1/2	Cyclin-dependent protein-serine kinase 1/2	Y15	Y15	PK007-2	T	T	T	34	27	NP_001777	P06493
CDK1/2	Cyclin-dependent protein-serine kinase 1/2	Y15	Y15	PK007-3	T	T	T	34	27	NP_001777	P06493
Cofilin 1	Cofilin 1	S3	S3	PN019	T	T	T	18	15	NP_005498	P23528
Cofilin 2	Cofilin 2	S3	S3	PN020	T	T	T	19	16	NP_068733	Q9Y281
Cortactin	Cortactin (amplaxin) (mouse)	Y470	Y466	PN022	T	T	T	62	77+82	NP_031829	Q60598
CREB1	cAMP response element binding protein 1	S129+S133	S129+S133	PN023	T	T	T	37	36	NP_004370	P16220
CREB1	cAMP response element binding protein 1	S133	S133	PN024	T	T	T	37	44	NP_004370	P16220
Crystallin αB	Crystallin alpha B (heat-shock 20 kDa like-protein)	S19	S19	PN025	T	T	T	20	18	NP_001876	P02511
Crystallin αB	Crystallin alpha B (heat-shock 20 kDa like-protein)	S45	S45	PN025	T	T	T	20	18	NP_001876	P02511
Dab1	Disabled homolog 1	Y198	Y198	PN026	T	T	T	60	79	NP_066566	O75553
Dok2	Docking protein 2 (mouse)		Y142	PN027	T	T	T	46	46	NP_034201	O60496
EGFR	Epidermal growth factor receptor-tyrosine kinase	Y1068	Y1068	PK009	T	T	T	134	175	NP_005219	P00533
EGFR	Epidermal growth factor receptor-tyrosine kinase	Y1148	Y1148	PK010	T	T	T	134	174	NP_005219	P00533

Target Protein	Target Protein Full Name	Phospho-site Human	Phospho-site Mouse	I.D. Code	Ab Reactivity Human	Ab Reactivity Mouse	Ab Reactivity Rat	Actual Mol. Mass Human	Obsv. Mol. Human	Link - Protein Human	Link - Swiss- Human
EGFR	Epidermal growth factor receptor-tyrosine kinase	Y1173	Y1173	PK011	T	T	T	**134**	**174**	NP_005219	
eIF2α	Eukaryotic translation initiation factor 2 alpha	S51	S52	PN028	T	T	T	**36**	**33**	NP_004085	P05198
eIF2α	Eukaryotic translation initiation factor 2 alpha	S51	S52	PN028	T	T	T	**36**	**33**	NP_004085	P05198
eIF2Bε	Eukaryotic translation initiation factor 2B epsilon	S540	S539	PN029	T	T	T	**80**	**79**	XP_291076	Q13144
eIF4E	Eukaryotic translation initiation factor 4 (mRNA cap binding protein)	S209	S209	PN030	T	T	T	**25**	**24**	NP_001959	P06730
eIF4E	Eukaryotic translation initiation factor 4 (mRNA cap binding protein)	S209	S209	PN030	T	T	T	**25**	**24**	NP_001959	P06730
eIF4G	Eukaryotic translation initiation factor 4 gamma 1	S1107	S1108	PN031	T	T	T	**176**	**192**	NP_004944	Q04637
eNos	Nitric-oxide synthase, endothelial	T494	T493	PN097	T	T	T	**130**	**130**	NP_000594.2	P29474
ErbB2	ErbB2 (Neu, HER2) receptor-tyrosine kinase	Y1139	Y1139	PK012-1	T	T	T	**138**	**160**	NP_004439	P04626
ErbB2	ErbB2 (Neu, HER2) receptor-tyrosine kinase	Y1139	Y1139	PK012-2	T	T	T	**138**	**160**	NP_004439	P04626
ErbB2	ErbB2 (Neu, HER2) receptor-tyrosine kinase	Y1248	Y1248	PK013-1	T	T	T	**138**	**182**	NP_004439	P04626
ErbB2	ErbB2 (Neu, HER2) receptor-tyrosine kinase	Y1248	Y1248	PK013-2	T	T	T	**138**	**182**	NP_004439	P04626
Erk1	Extracellular regulated protein-serine kinase 1 (p44 MAP kinase)	T202+Y204	T202+Y204	PK014-1	T	T	T	**43**	**41**	AAA36142.1	P27361
Erk1	Extracellular regulated protein-serine kinase 1 (p44 MAP kinase)	T202+Y204	T202+Y204	PK014-2	T	T	T	**43**	**41**	AAA36142.1	P27361
Erk1	Extracellular regulated protein-serine kinase 1 (p44 MAP kinase)	T202+Y204	T202+Y204	PK014-3	T	T	T	**43**	**41**	AAA36142.1	P27361
Erk2	Extracellular regulated protein-serine kinase 1 (p44 MAP kinase)	T202+Y204	T202+Y204	PK015-1	T	T	T	**43**	**41**	AAA36142.1	P27361
Erk2	Extracellular regulated protein-serine kinase 1 (p44 MAP kinase)	T202+Y204	T202+Y204	PK015-2	T	T	T	**43**	**41**	AAA36142.1	P27361
Erk2	Extracellular regulated protein-serine kinase 1 (p44 MAP kinase)	T202+Y204	T202+Y204	PK015-3	T	T	T	**43**	**41**	AAA36142.1	P27361
Erk5	Extracellular regulated protein-serine kinase 5 (Big MAP kinase 1 (BMK1))	T218+Y220	T218+Y220	PK016	T	T	T	**89**	**130**	NP_620602	P53778
FAK	Focal adhesion protein-tyrosine kinase	S722	S722	PK020	T	T	T	**119**	**115**	NP_005598	Q05397
FAK	Focal adhesion protein-tyrosine kinase	S732	S732	PK021	T	T	T	**119**	**125**	NP_005598	Q05397
FAK	Focal adhesion protein-tyrosine kinase	S843	S843	PK022	T	T	T	**119**	**113**	NP_005598	Q05397
FAK	Focal adhesion protein-tyrosine kinase	S910	S910	PK024	T	T	T	**119**	**114**	NP_005598	Q05397
FAK	Focal adhesion protein-tyrosine kinase	Y397	Y397	PK017-1	T	T	T	**119**	**113**	NP_005598	Q05397
FAK	Focal adhesion protein-tyrosine kinase	Y397	Y397	PK017-2	T	T	T	**119**	**113**	NP_005598	Q05397
FAK	Focal adhesion protein-tyrosine kinase	Y576	Y576	PK018-1	T	T	T	**119**	**114**	NP_005598	Q05397
FAK	Focal adhesion protein-tyrosine kinase	Y576	Y576	PK018-2	T	T	T	**119**	**114**	NP_005598	Q05397
FAK	Focal adhesion protein-tyrosine kinase	Y577	Y577	PK019	T	T	T	**119**	**113**	NP_005598	Q05397
FAK	Focal adhesion protein-tyrosine kinase	Y861	Y861	PK023	T	T	T	**119**	**117**	NP_005598	Q05397
FKHRL1	Forkhead-like transcription factor 1 (FOXO3A)	T32	T32	PN032	T	F	T	**71**	**99**	NP_001446	O43524
Fos	Fos-c FBJ murine osteosarcoma oncoprotein-related transcription factor	T232	T232	PN033	T	T	T	**41**	**57**	NP_005243	P01100
GAP-43	Growth associated protein 43 (Neuromodulin)	S41	S41	PN098	T	T	T	**25**	**25**	NP_002036.1	P17677
GFAP	Glial fibrillary acidic protein	S8	S8	PN034	T	T	T	**50**	**50**	NP_002046	P14136
GRK2 [BARK1]	G protein-coupled receptor-serine kinase 2	S670	S670	PK025	T	T	T	**80**	**77+65**	NP_001610	P25098
GSK3α	Glycogen synthase-serine kinase 3 alpha	S21	S21	PK026-1	T	T	T	**51**	**45**	NP_063937	P49840
GSK3α	Glycogen synthase-serine kinase 3 alpha	Y279	Y279	PK026-2	T	T	T	**51**	**45**	NP_063937	P49840
GSK3α	Glycogen synthase-serine kinase 3 alpha	Y279	Y279	PK026-3	T	T	T	**51**	**45**	NP_063937	P49840
GSK3β	Glycogen synthase-serine kinase 3 beta	S9	S9	PK027-1	T	T	T	**47**	**40**	NP_002084	P49841
GSK3β	Glycogen synthase-serine kinase 3 beta	Y216	Y216	PK027-2	T	T	T	**47**	**40**	NP_002084	P49841
GSK3β	Glycogen synthase-serine kinase 3 beta	Y216	Y216	PK027-3	T	T	T	**47**	**40**	NP_002084	P49841
GYS1	Human muscle glycogen synthase	S641	S641	PN099	T	T	T	**84**	**84**	NP_002094.2	P13807
Histone H1	Histone H1 phosphorylated	CDK1 sites	CDK1 sites	PN035	T	T	T	**22**	**30**	NP_005316	Q02539
Histone H2A.X	Histone H2A variant X	S139	S139	PN036	T	T	T	**15**	**14**	NP_002096	P16104
Histone H2B	Histone H2B	S14	S14	PN037	T	T	T	**14**	**14**	NP_778225	P33778
Histone H3	Histone H3.3	S10	S10	PN038	T	T	T	**15**	**14**	NP_003521	P84243
Histone H3	Histone H3.3	S28	S28	PN039	T	T	T	**15**	**14**	NP_003521	P84243
Histone H3	Histone H3.3	T11	T11	PN100	T	T	T	**15**	**14**	NP_003521	P84243

Target Protein	Target Protein Full Name	Phospho-site	Phospho-site	I.D. Code	Ab Reactivity			Actual Mol. Mass	Obsv. Mol.	Link - Protein	Link - Swiss-
		Human	Mouse		Human	Mouse	Rat	Human	Human	Human	Human
Histone H3	Histone H3.3	T3	T3	PN101	T	T	T	**15**	**14**	NP_003521	P84243
Hsp25	Heat shock 27 kDa protein beta 1	S86	S86	PN102	T	T	T	**23**	**23**	NP_038588.1	P14602
Hsp27	Heat shock 27 kDa protein beta 1 (HspB1)	S15	S15	PN040	T	F	T	**23**	**23**	NP_001531	P04792
Hsp27	Heat shock 27 kDa protein beta 1 (HspB1)	S15	S15	PN040	T	F	T	**23**	**23**	NP_001531	P04792
Hsp27	Heat shock 27 kDa protein beta 1 (HspB1)	S78	S78	PN041	T	F	T	**23**	**23**	NP_001531	P04792
Hsp28	Heat shock 27 kDa protein beta 1 (HspB1)	S82	S82	PN042	T	T	T	**23**	**22**	NP_001531	P04792
Hsp29	Heat shock 27 kDa protein beta 1 (HspB1)	S82	S82	PN042	T	T	T	**23**	**22**	NP_001531	P04792
Huntington	Huntington's disease protein	S421	S398	PN103	T	T	T	**350**	**350**	NP_002102.4	P42858
IKKα	Inhibitor of NF-kappa-B protein-serine kinase alpha (CHUK)	S180	S180	PK030	T	T	T	**85**	**80**	NP_001269	O15111
IKKβ	Inhibitor of NF-kappa-B protein-serine kinase beta	S181	S181	PK030	T	T	T	**87**	**90**	NP_001547	O15111
Integrin α4	Integrin alpha 4 (VLA4)	S988	S988	PN043	T	T	T	**115**	**154**	NP_000876	P13612
Integrin β1	Integrin beta 1 (fibronectin receptor beta subunit, CD29 antigen)	S785	S785	PN044	T	T	T	**88**	**146**	NP_002202	P05556
Integrin β1	Integrin beta 1 (fibronectin receptor beta subunit, CD29 antigen)	Y783	Y783	PN105	T	T	T	**88**	**146**	NP_002202	P05556
IR [INSR]	Insulin receptor	Y999	Y972	PK032	T	T	T	**156**	**83**	NP_000199	P06213
IR/IGF1R [INSR]	Insulin receptor / Insulin-like growth factor 1 receptor	Y1189/ Y1190	Y1162/ Y1163	PK033	T	T	T	**156/ 155**	**95**	NP_000866	P06213
IRS1	Insulin receptor substrate 1	Y1179	Y1179	PN046	T	T	T	**132**	**181**	NP_005535	P35568
IRS1	Insulin receptor substrate 1	Y612	Y612	PN045	T	T	T	**132**	**173**	NP_005535	P35568
JAK2	Janus protein-tyrosine kinase 2	Y1007/ Y1008	Y1007/ Y1008	PK034	T	T	T	**131**	**119**	NP_004963	O60674
JNK	Jun N-terminus protein-serine kinase (stress-activated protein kinase (SAPK))	T183+Y185	T183+Y185	PK035-1	T	T	T	**44 + 48 + 53**	**48+44+ 39+37**	NP_002741	P45983
JNK	Jun N-terminus protein-serine kinase (stress-activated protein kinase (SAPK))	T183+Y185	T183+Y185	PK035-2	T	T	T	**44 + 48 + 53**	**48+44+ 39+37**	NP_002741	P45983
JNK	Jun N-terminus protein-serine kinase (stress-activated protein kinase (SAPK))	T183+Y185	T183+Y185	PK035-3	T	T	T	**44 + 48 + 53**	**48+44+ 39+37**	NP_002741	P45983
Jun	Jun proto-oncogene-encoded AP1 transcription factor	S63	S63	PN047	T	T	T	**36**	**40+39+ 38**	NP_002219	P05412
Jun	Jun proto-oncogene-encoded AP1 transcription factor	S73	S73	PN048-1	T	T	T	**36**	**43+40+ 38**	NP_002219	P05412
Jun	Jun proto-oncogene-encoded AP1 transcription factor	S73	S73	PN048-2	T	T	T	**36**	**43+40+ 38**	NP_002219	P05412
Jun	Jun proto-oncogene-encoded AP1 transcription factor	S73	S73	PN048-3	T	T	T	**36**	**43+40+ 38**	NP_002219	P05412
Kit	Kit/Steel factor receptor-tyrosine kinase	Y703	Y703	PK036	T	T	F	**110**	**141**	P10721	P10721
Kit	Kit/Steel factor receptor-tyrosine kinase	Y730	Y730	PK037	T	T	T	**110**	**134 + 187**	P10721	P10721
Kit	Kit/Steel factor receptor-tyrosine kinase	Y936	Y936	PK038	T	T	F	**110**	**183**	P10721	P10721
Lck	Lymphocyte-specific protein-tyrosine kinase	S157	S158	PK039	T	T	T	**58**	**46 + 54**	NP_005347	P06239
Lck	Lymphocyte-specific protein-tyrosine kinase	Y191	Y192	PK040	T	T	T	**58**	**46**	NP_005347	P06239
Lck	Lymphocyte-specific protein-tyrosine kinase	Y504	Y505	PK041	T	T	F	**58**	**46**	NP_005347	P06239
LIMK1/2	LIM domain kinase 1/2	Y508/T505	Y507/T508	PK042	T	T	T	**73 / 72**		NP_002305	P53667
Lyn	Yes-related protein-tyrosine kinase	Y507	Y507	PK043	T	T	T	**58**	**46**	NP_002341	P07948
MAPKAPK2	Mitogen-activated protein kinase-activated protein kinase 2	T222	T222	PK044	T	T	T	**46**	**51**	NP_004750	P49137
MAPKAPK2	Mitogen-activated protein kinase-activated protein kinase 2	T334	T334	PN049-1	T	T	T	**46**	**45**	NP_004750	P49137
MAPKAPK2	Mitogen-activated protein kinase-activated protein kinase 2	T334	T334	PN049-2	T	T	T	**46**	**45**	NP_004750	P49137
MARCKS	Myristoylated alanine-rich protein kinase C substrate	S158+S162	S158+S162	PN050-1	T	T	T	**31**	**88+83**	NP_002347	P29966
MARCKS	Myristoylated alanine-rich protein kinase C substrate	S158+S162	S158+S162	PN050-2	T	T	T	**31**	**88+83**	NP_002347	P29966
MEK1 [MAP2K1]	MAPK/ERK protein-serine kinase 1 (MKK1)	S297	S298	PK047-1	T	T	T	**43**	**42**	NP_002746	Q02750
MEK1 [MAP2K1]	MAPK/ERK protein-serine kinase 1 (MKK1)	S297	S298	PK047-2	T	T	T	**43**	**42**	NP_002746	Q02750
MEK1 [MAP2K1]	MAPK/ERK protein-serine kinase 1 (MKK1)	T291	T292	PK046-1	T	T	T	**43**	**42**	NP_002746	Q02750
MEK1 [MAP2K1]	MAPK/ERK protein-serine kinase 1 (MKK1)	T291	T292	PK046-2	T	T	T	**43**	**42**	NP_002746	Q02750
MEK1 [MAP2K1]	MAPK/ERK protein-serine kinase 1 (MKK1)	T291	T292	PK046-3	T	T	T	**43**	**42**	NP_002746	Q02750
MEK1 [MAP2K1]	MAPK/ERK protein-serine kinase 1 (MKK1)	T385	T386	PK048-1	T	T	T	**43**	**42**	NP_002746	Q02750
MEK1 [MAP2K1]	MAPK/ERK protein-serine kinase 1 (MKK1)	T385	T386	PK048-2	T	T	T	**43**	**42**	NP_002746	Q02750
MEK1 [MAP2K1]	MAPK/ERK protein-serine kinase 1 (MKK1)	T385	T386	PK048-3	T	T	T	**43**	**42**	NP_002746	Q02750

Target Protein	Target Protein Full Name	Phospho-site	Phospho-site	I.D. Code	Ab Reactivity			Actual Mol. Mass	Obsv. Mol.	Link - Protein	Link - Swiss-
		Human	Mouse		Human	Mouse	Rat	Human	Human	Human	Human
MEK1 [MAP2K1]	MAPK/ERK protein-serine kinase 1 (MKK1)	S217+S221	S217+S221	PK045	T	T	T	**43**	**42**	NP_002746	Q02750
MEK2 [MAP2K2]	MAPK/ERK protein-serine kinase 2 (MKK2) (human)	T394	T395	PK049	T	F	F	**44**	**42**	AAH00471.1	P36507
MEK2 [MAP2K2]	MAPK/ERK protein-serine kinase 2 (MKK2) (mouse)	T394	T395	PK050	F	T	T	**44**	**42**	NP_075627	P36507
MEK3 [MAP2K3]	MAP kinase protein-serine kinase 3 (MKK3)	S189	S218	PK051	T	T	T	**36**	**35**	NP_002747	P46734
MEK4 [MAP2K4]	MAP kinase protein-serine kinase 4 (MKK4)	S257+T261	S257+T261	PK052	T	T	T	**44**	**41**	NP_003001	P45985
MEK6 [MAP2K6]	MAP kinase protein-serine kinase 6 (MKK6)	S207	S207	PK053	T	T	T	**37 + 31**	**35**	NP_002749	P46734
Met	Hepatocyte growth factor (HGF) receptor-tyrosine kinase	Y1003	Y1001	PK054	T	T	T	**156**	**154**	NP_000236	P08581
Met	Hepatocyte growth factor (HGF) receptor-tyrosine kinase	Y1230+ Y1234+	Y1228+ Y1232+	PK055	T	T	T	**156**	**158**	NP_000236.	P08581
MLK3	Mixed-lineage protein-serine kinase 3	T277+S281	T278+S282	PK056	T	T	T	**93**	**133**	NP_002410	Q16584
Mnk1	MAP kinase-interacting protein-serine kinase 1 (calmodulin-activated)	T209+T214	T197+T202	PK057	T	T	T	**47**	**48**	NP_003675	Q9BUB5
MRLC2	Myosin regulatory light chain isoform 1	S18	S19	PN051-1	T	T	T	**20**	**20**	NP_291024	P19105
MRLC2	Myosin regulatory light chain isoform 1	S18	S19	PN051-2	T	T	T	**20**	**20**	NP_291024	P19105
Msk1	Mitogen & stress-activated protein-serine kinase 1	S376	S375	PK058	T	T	T	**90**	**71+78**	NP_004746	O75582
mTOR [FRAP]	Mammalian target of rapamycin (FRAP)	S2448	S2448	PK116	T	T	T	**289**	**199**	NP_004949	P42345
MYPT1	Myosin phosphatase target 1	T696	T694	PN052	T	T	T	**115**	**141**	NP_446342	O14974
NFkappaB p65	NF-kappa-B p65 nuclear transcription factor	S276	S276	PN053	T	T	T	**64**	**64**	NP_003989	Q04206
NMDAR2B	N-methyl-D-aspartate (NMDA) glutamate receptor 2B subunit	Y1474	Y1474	PN054	T	T	T	**166**	**166**	NP_000825	Q13224
NR1	N-methyl-D-aspartate (NMDA) glutamate receptor 1 subunit zeta	S896	S896	PN055	T	T	T	**105**	**109**	NP_000823	Q05586
p27 Kip1	p27 cyclin-dependent kinase inhibitor 1B	T187	T187	PN056	T	T	T	**22**	**26**	NP_004055	P46527
p38α MAPK	Mitogen-activated protein-serine kinase p38 alpha	T180+Y182	T180+Y182	PK060-1	T	T	T	**41**	**40+38+ 36**	NP_001306	Q16539
p38α MAPK	Mitogen-activated protein-serine kinase p38 alpha	T180+Y182	T180+Y182	PK060-2	T	T	T	**41**	**40+38+ 36**	NP_001306	Q16539
p38α MAPK	Mitogen-activated protein-serine kinase p38 alpha	T180+Y182	T180+Y182	PK060-3	T	T	T	**41**	**40+38+ 36**	NP_001306	Q16539
p38α MAPK	Mitogen-activated protein-serine kinase p38 alpha	T180+Y182	T180+Y182	PK060-4	T	T	T	**41**	**40+38+ 36**	NP_001306	Q16539
p53	Tumor suppressor protein p53 (antigenNY CO-13)	S392	S389	PN057-1	T	T	F	**44**	**49**	NP_000537	P04637
p53	Tumor suppressor protein p53 (antigenNY CO-13)	S392	S389	PN057-2	T	T	F	**44**	**49**	NP_000537	P04637
p53	Tumor suppressor protein p53 (antigenNY CO-13)	S392	S389	PN057-3	T	T	F	**44**	**49**	NP_000537	P04637
PAK1/2/3	p21-activated protein-serine kinase 1/2/3	S144/S141/S 154	S144/S141/ S154	PK061	T	T	T	**61/ 58 / 61**	**58 / 53**	NP_002567	Q13153
Pax2	Paired box protein 2	S394	S393	PN058	T	T	T	**45**	**37**	Q02962	Q02962
Paxillin 1	Paxillin 1	Y118	Y118	PN060-1	T	T	T	**65**	**69**	NP_002850	P49023
Paxillin 1	Paxillin 1	Y118	Y118	PN060-2	T	T	T	**65**	**69**	NP_002850	P49023
Paxillin 1	Paxillin 1	Y31	Y31	PN059	T	T	T	**65**	**70**	NP_002850	P49023
PDGFRα	Platelet-derived growth factor receptor kinase alpha	Y742	Y742	PK062	T	T	T	**123**	**176**	NP_006197	P16234
PDGFRα	Platelet-derived growth factor receptor kinase alpha	Y754	Y754	PK063	T	T	T	**123**	**180**	NP_006197	P16234
PDGFRα/β	Platelet-derived growth factor receptor kinase alpha/beta	aY572+Y574 /bY579+	aY572+Y574 /bY579+	PK064	T	T	T	**123 / 124**	**180**	NP_006197	P16234
PDGFRβ	Platelet-derived growth factor receptor kinase beta	Y716	Y715	PK065	T	T	T	**123 / 124**	**180**	NP_032835	P09619
PDK1	3-Phosphoinositide-dependent protein-serine kinase 1	S244	S241	PK066	T	T	T	**63**	**56/59**	NP_002604	O15530
PED15 (PEA15)	Phosphoprotein-enriched in diabetes/astrocytes 15	S116	S116	PN061	T	T	T	**15**	**12**	NP_003759	Q15121
PKA Cα/β	cAMP-dependent protein-serine kinase catalytic subunit alpha/beta	T197	T197	PK067	T	T	T	**40 / 40**	**39**	NP_002721	P17612
PKA Cβ	cAMP-dependent protein-serine kinase catalytic subunit beta	S338	S338	PK068	T	T	T	**40**	**39**	NP_002722	P22694
PKA R2α	cAMP-dependent protein-serine kinase regulatory type 2 subunit alpha	S98	S95	PK069	T	T	T	**45**	**58**	NP_523671	P13861
PKA R2β	cAMP-dependent protein-serine kinase regulatory type 2 subunit beta	S114	S114	PK070	T	T	T	**46**	**38**	NP_004148	P31323
PKBα [Akt1]	Protein-serine kinase B alpha (Akt1)	S473	S473	PK072-1	T	T	T	**56**	**56/59**	NP_005154	P31749
PKBα [Akt1]	Protein-serine kinase B alpha (Akt1)	S473	S473	PK072-2	T	T	T	**56**	**56/59**	NP_005154	P31749
PKBα [Akt1]	Protein-serine kinase B alpha (Akt1)	S473	S473	PK072-3	T	T	T	**56**	**56/59**	NP_005154	P31749
PKBα [Akt1]	Protein-serine kinase B alpha (Akt1)	T308	T308	PK071-1	T	T	T	**56**	**56/60**	NP_005154	P31749
PKBα [Akt1]	Protein-serine kinase B alpha (Akt1)	T308	T308	PK071-2	T	T	T	**56**	**56/60**	NP_005154	P31749

Target Protein	Target Protein Full Name	Phospho-site	Phospho-site	I.D. Code	Ab Reactivity			Actual Mol. Mass	Obsv. Mol.	Link - Protein	Link - Swiss-
		Human	Mouse		Human	Mouse	Rat	Human	Human	Human	Human
PKCα	Protein-serine kinase C alpha	S657	S657	PK073	T	T	T	**77**	**79**	NP_002728	P17252
PKCα/β2	Protein-serine kinase C alpha/beta 2	T638/T641	T638/T641	PK074	T	T	T	**77 / 77**	**78/80**	NP_002728	P17252
PKCβ1/2	Protein-serine kinase C beta 1/2	T500	T500	PK075	T	T	T	**77 / 77**	**79**	NP_997700	P05771
PKCβ2	Protein-serine kinase C beta 2	T641	T641	PK076	T	T	T	**77**	**79**	NP_002729	P05771
PKCδ	Protein-serine kinase C delta	S645	S643	PK079	T	T	T	**77**	**74**	NP_006245	Q05655
PKCδ	Protein-serine kinase C delta	S664	S662	PK080	T	T	T	**77**	**74**	NP_006245	Q05655
PKCδ	Protein-serine kinase C delta	T507	T505	PK078	T	T	T	**77**	**70+74**	NP_006245	Q05655
PKCδ	Protein-serine kinase C delta	Y313	Y311	PK077-1	T	T	T	**77**	**74**	NP_006245	Q05655
PKCδ	Protein-serine kinase C delta	Y313	Y311	PK077-2	T	T	T	**77**	**74**	NP_006245	Q05655
PKCε	Protein-serine kinase C epsilon	S729	S729	PK081-1	T	T	T	**84**	**91**	NP_005391	Q02156
PKCε	Protein-serine kinase C epsilon	S729	S729	PK081-2	T	T	T	**84**	**91**	NP_005391	Q02156
PKCγ	Protein-serine kinase C gamma	T514	T514	PK082-1	T	T	T	**78**	**78/81**	NP_002730	P05129
PKCγ	Protein-serine kinase C gamma	T514	T514	PK082-2	T	T	T	**78**	**78/81**	NP_002730	P05129
PKCγ	Protein-serine kinase C gamma	T655	T655	PK083	T	T	T	**78**	**78/81**	NP_002730	P05129
PKCγ	Protein-serine kinase C gamma	T674	T674	PK084	T	T	T	**78**	**78/81**	NP_002730.1	P05129
PKCη	Protein-serine kinase C eta	S674	S674	PK086	T	T	T	**78**	**79**	NP_006246	P24723
PKCη	Protein-serine kinase C eta	T655	T655	PK085	T	T	T	**78**	**79**	NP_006246	P24723
PKCλ/ι	Protein-serine kinase C lambda/iota	T555	T554	PK087	T	T	T	**67**	**79**	NP_002731	P41743
PKCθ	Protein-serine kinase C theta	S676	S676	PK089	T	T	T	**82**	**74**	NP_006248	Q04759
PKCθ	Protein-serine kinase C theta	S695	S695	PK090	T	T	T	**82**	**74**	NP_006248	Q04759
PKCθ	Protein-serine kinase C theta	T538	T538	PK088	T	T	T	**82**	**74**	NP_006248	Q04759
PKCζ/λ	Protein-serine kinase C zeta/lambda	T410/T403	T410/T402	PK091	T	T	T	**68 / 67**	**79**	NP_002735	Q05513
PKD (PKCμ)	Protein-serine kinase C mu (Protein kinase D)	S738+S742	S744+S748	PK092	T	T	T	**102**	**122**	NP_002733	Q15139
PKD (PKCμ)	Protein-serine kinase C mu (Protein kinase D)	S910	S916	PK093-1	T	T	T	**102**	**122**	NP_002733	Q15139
PKD (PKCμ)	Protein-serine kinase C mu (Protein kinase D)	S910	S916	PK093-2	T	T	T	**102**	**122**	NP_002733	Q15139
PKR1	Double-stranded RNA-dependent protein-serine kinase	T451	T414	PK094	T	T	T	**62**	**76+69**	NP_002750	P19525
Plk1	Polo-like protein-serine kinase 1	T210	T210	PK117	T	T	T	**68**	**68**	NP_005021.2	P53350
PP1/Cα	Protein-serine phosphatase 1 - catalytic subunit - alpha isoform	T320	T320	PP001	T	T	T	**38**	**35**	NP_002699	P62136
PRAS40	Proline-rich Akt substrate 40 kDa (Akt1S1)	T246	T247	PN062	T	T	T	**27**	**44**	NP_115751	Q96B36
PRK1 [PKN1]	Protein kinase C-related protein-serine kinase 1	T774	T778	PK095	T	T	T	**104**	**126**	NP_002732	Q16512
PRK2 [PKN2]	Protein kinase C-related protein-serine kinase 2	T816	none	PK096	T	T	T	**112**	**135**	NP_006247	Q16512
Progesterone Receptor	Progesterone receptor	S294	S294	PN104	T	T	T	**100**	**100**	NP_000917.3	P06401
PTEN	Phosphatidylinositol-3,4,5-trisphosphate 3-phosphatase and protein phosphatase	S370	S370	PP002	T	T	T	**47**	**53**	NP_000305	P60484
PTEN	Phosphatidylinositol-3,4,5-trisphosphate 3-phosphatase and protein phosphatase	S380+T382+S385	S380+T382+S385	PP003	T	T	T	**47**	**55**	NP_000305	P60484
Pyk2	Protein-tyrosine kinase 2	Y579	Y579	PK097	T	T	F	**116**	**122**	NP_775268	Q14289
Rac1/cdc42	Ras-related C3 botulinum toxin substrate 1	S71	S71	PN063	T	T	T	**21**	**21**	NP_008839	P60953
Rad17	Rad17 homolog	S645	S657	PN064	T	T		**77**	**58+64+68**	NP_579921	O75943
Raf1	Raf1 proto-oncogene-encoded protein-serine kinase	S259	S259	PK098	T	T	T	**84**	**63+68**	NP_002871	P04049
Rb	Retinoblastoma-associated protein 1	S612	S605	PN066	T	T	T	**106**	**127**	NP_000312	P06400
Rb	Retinoblastoma-associated protein 1	S780	S773	PN067	T	T	T	**106**	**127**	NP_000312	P06400
Rb	Retinoblastoma-associated protein 1	S807	S800	PN068	T	T	T	**106**	**127**	NP_000312	P06400
Rb	Retinoblastoma-associated protein 1	S807+S811	S800+S804	PN069	T	T	T	**106**	**127**	NP_000312	P06400
Rb	Retinoblastoma-associated protein 1	T356	T350	PN065	T	T	T	**106**	**127**	NP_000312	P06400
Rb	Retinoblastoma-associated protein 1	T821	T814	PN070	T	T	T	**106**	**127**	NP_000312	P06400
Rb	Retinoblastoma-associated protein 1	T826	T819	PN071	T	T	T	**106**	**127**	NP_000312	P06400
Ret	Ret receptor-tyrosine kinase	S696	S696	PN072	T	T	T	**124**	**186**	NP_065681	P07949
RSK1/2	Ribosomal S6 protein-serine kinase 1/2	S380/S386	S380/S386	PK101-1	T	T	T	**83 / 84**	**89+78+70**	NP_002944	Q15418

Target Protein	Target Protein Full Name	Phospho-site Human	Phospho-site Mouse	I.D. Code	Ab Reactivity Human	Ab Reactivity Mouse	Ab Reactivity Rat	Actual Mol. Mass Human	Obsv. Mol. Human	Link - Protein Human	Link - Swiss- Human
RSK1/2	Ribosomal S6 protein-serine kinase 1/2	S221/S227	S221/S227	PK099	T	T	T	**83 / 84**	**89+78+70**	NP_002944	Q15418
RSK1/2	Ribosomal S6 protein-serine kinase 1/2	S363/S369	S363/S369	PK100	T	T	T	**83 / 84**	**89+78+70**	NP_002944	Q15418
RSK1/2	Ribosomal S6 protein-serine kinase 1/2	S380/S386	S380/S386	PK101-2	T	T	T	**83 / 84**	**89+78+70**	NP_002944	Q15418
RSK1/2	Ribosomal S6 protein-serine kinase 1/2/3	T573/T577/T570	T573/T577/T570	PK102	T	T	T	**83 / 84**	**89+78+70**	NP_002944	Q15418
RSK1/3	Ribosomal S6 protein-serine kinase 1/3	T359+S363/T356+S360	T359+S363/T356+S360	PK103	T	T	T	**83 / 84**	**89+78+70**	NP_002944	Q15418
S6	40S ribosomal protein S6	S235	S235	PN073	T	T	T	**29**	**38**	NP_001001	P62753
S6Kα	p70 ribosomal protein-serine S6 kinase alpha	T229	T252	PK104	T	T	T	**56**	**80**	NP_003152	P23443
S6Kα	p70 ribosomal protein-serine S6 kinase alpha	T421+S424	T444+S447	PK106	T	T	T	**56**	**62+69+86**	NP_003152	P23443
S6Kα	p70 ribosomal protein-serine S6 kinase alpha	T389	T412	PK105	T	T	T	**56**	**69**	NP_003152	P23443
Shc1	SH2 domain-containing transforming protein 1	Y349+Y350	Y349+Y350	PN074	T	T	T	**63**	**68+49**	NP_003020	P29353
SHP2	Protein-tyrosine phosphatase 1D (SHP2, SHPTP2, Syp, PTP2C)	S576	S580	PP004	T	T	T	**68**	**48+70**	NP_002825	Q06124
Smad1/5/9	SMA- and mothers against decapentaplegic homologs 1/5/9	S463+S465/S463+S465	S463+S465/S463+S465/	PN075	T	T	T	**52 / 52 / 52**	**65**	NP_005891	Q15797
Smad2	SMA- and mothers against decapentaplegic homolog 2	S465+S467	S465/S467	PN076	T	T	T	**52**	**53**	NP_001003652	Q15796
SOX9	SRY (sex determining region Y)-box 9 (campomelic dysplasia, autosomal sex-	S181	S181	PN077	T	T	T	**56**	**48**	NP_000337	P48436
Src	Src proto-oncogene-encoded protein-tyrosine kinase	Y418	Y423	PK107	T	T	T	**60**	**49**	NP_005408	P12931
Src	Src proto-oncogene-encoded protein-tyrosine kinase	Y529	Y534	PK108	T	T	T	**60**	**48+46**	NP_005408	P12931
STAT1	Signal transducer and activator of transcription 1	S727	S727	PN078	T	T	T	**87**	**83**	NP_009330	P42224
STAT1	Signal transducer and activator of transcription 1	Y701	Y701	PN079-1	T	T	T	**87**	**86**	NP_009330	P42224
STAT1	Signal transducer and activator of transcription 1	Y701	Y701	PN079-2	T	T	T	**87**	**86**	NP_009330	P42224
STAT2	Signal transducer and activator of transcription 2	Y690	Y688	PN080	T	T	T	**98**	**113**	NP_005410	P52630
STAT3	Signal transducer and activator of transcription 3	S727	S727	PN081	T	T	T	**88**	**81**	NP_003141	P40763
STAT3	Signal transducer and activator of transcription 3	Y705	Y705	PN082	T	T	T	**88**	**81**	NP_003141	P40763
STAT5A	Signal transducer and activator of transcription 5A	Y694	Y694	PN083	T	T	T	**91**	**93**	NP_003143	P42229
Syk	Spleen protein-tyrosine kinase	Y352	Y346	PK109	T	T	T	**72**	**71**	NP_003168	
Synapsin 1	Synapsin 1 isoform Ia	S605	S605	PN105	T	F	F	**74**	**73**	NP_008881	P17600
Synapsin 1	Synapsin 1 isoform Ia	S9	S9	PN084	T	F	F	**74**	**73**	NP_008881	P17600
Tau	Microtubule-associated protein tau	S518	S493	PN106	T	T	T	**79**	Multiple bands	NP_005901	P10636
Tau	Microtubule-associated protein tau	S738	S713	PN107	T	T	T	**78**	Multiple bands	NP_005901	P10636
Tau	Microtubule-associated protein tau	S515	S490	PN085	T	T	T	**79**	Multiple bands	NP_005901	P10636
Tau	Microtubule-associated protein tau	S515+S518	S490+S493	PN086	T	T	T	**79**	Multiple bands	NP_005901	P10636
Tau	Microtubule-associated protein tau	S530	S505	PN088	T	T	T	**79**	Multiple bands	NP_005901	P10636
Tau	Microtubule-associated protein tau	S578	S553	PN089	T	T	T	**79**	Multiple bands	NP_005901	P10636
Tau	Microtubule-associated protein tau	S712	S687	PN090	T	T	T	**79**	Multiple bands	NP_005901	P10636
Tau	Microtubule-associated protein tau	S716	S691	PN091	T	T	T	**79**	Multiple bands	NP_005901	P10636
Tau	Microtubule-associated protein tau	S720	S695	PN092	T	T	T	**79**	Multiple bands	NP_005901	P10636
Tau	Microtubule-associated protein tau	T547	T547	PN108	T	T	T	**80**	Multiple bands	NP_005901	P10636
Tyrosine Hydroxylase	Tyrosine hydroxylase isoform a	S18	S19	PN109	T	T	T	**59**	**68**	NP_954986	P07101
Tyrosine Hydroxylase	Tyrosine hydroxylase isoform a	S70	S40	PN093	T	T	T	**59**	**68**	NP_954986	P07101
VEGFR2 [KDR]	Vascular endothelial growth factor receptor-tyrosine kinase 2 (Flk1)	Y1054	Y1052	PK110	T	T	T	**152**	**226**	NP_002244	P35968
VEGFR2 [KDR]	Vascular endothelial growth factor receptor-tyrosine kinase 2 (Flk1)	Y1054+Y1059	Y1052+Y1057	PK111	T	T	T	**152**	**226**	NP_002244	P35968
Vimentin	Vimentin	S33	S33	PN094	T	T	T	**54**	**54**	NP_003371	P08670
Vinculin	Vinculin	Y821	Y821	PN095	T	T	T	**124**	**112**	NP_003364	P18206
ZAP70	Zeta-chain (TCR) associated protein-tyrosine kinase, 70 kDa	Y292	Y290	PK112	T	T	T	**70**	**71**	NP_001070	P43403
ZAP70	Zeta-chain (TCR) associated protein-tyrosine kinase, 70 kDa	Y315+Y319	Y315+Y319	PK113	T	T	T	**70**	**71**	NP_001070	P43403
ZAP70	Zeta-chain (TCR) associated protein-tyrosine kinase, 70 kDa	Y319	Y319	PK114	T	T	T	**70**	**71**	NP_001070	P43403

KINEXUS

SERVICE ORDER FORM

Form: CKSP-SOF-01

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 KINASE SUBSTRATE PROFILING REPORTS

RESULTS SENT BY EMAIL TO: ❑ AUTHORIZED REPRESENTATIVE/INVESTIGATOR **AND/OR** ❑ CONTACT PERSON

BILLING INFORMATION

The Custom Kinase Substrate Profiling Service is offered for the detection of physiological substrates of purified active protein kinases in cell/tissue lysates. Each complete analysis is performed with one protein kinase and one cell/tissue lysate subjected to antibody microarray analysis with follow up on substrate leads by Western blotting. Each Kinex™ Phospho-Antibody Microarray is analyzed with the lysate incubated in the absence and presence of the protein kinase. Each immunoblotting analysis is performed with the lysate incubated in both the absence and presence of the protein kinase and probing with 18 phospho-antibodies.

Cost Breakdown ***All prices in U.S. Funds***

1. Customer supplied cell/tissue lysate. Number of lysates =	_____	X 0	= $ No charge
2. Kinexus supplied cell lysate (choose from Appendix 2). Number of lysates =	_____	X $499.00	= $
3. Customer supplied purified protein kinase. Number of kinases =	_____	X 0	= $ No charge
4. Kinexus supplied purified kinase (choose from Appendix 1). Number of kinases =	_____	X $200.00	= $
Kinexus supplied purified kinase (choose from Appendix 1). Number of kinases =	_____	X $400.00	= $
Kinexus supplied purified kinase (choose from Appendix 1). Number of kinases =	_____	X $600.00	= $
5. Number of Non-confidential phospho-Ab microarray and immunoblot analyses =	_____	X $2795.00	= $
6. Number of Confidential phospho-Ab microarray and immunoblot analyses =	_____	X $4665.00	= $

***Quotation or Reference Number*:** _____ - $ _____

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 SERVICE AGREEMENT AND AGREES TO BE BOUND BY THE TERMS AND CONDITIONS:

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

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

Form: CKSP-SIF-01

CUSTOM KINASE SUBSTRATE PROFILING SERVICE IDENTIFICATION FORM

Subject to terms of the Kinexus Service Agreement

KINEXUS ORDER NUMBER

NAME: _____ **COMPANY/INSTITUTE:** _____

(Authorized Representative or Principal Investigator)

CUSTOM KINASE SUBSTRATE PROFILING SERVICE REQUESTED: (WITH LYSATES AND PROTEIN KINASES FROM EITHER THE CLIENT OR KINEXUS)

Use this form to order the Custom Kinase Substrate Profiling Service offered by Kinexus. Complete Box B only if you are providing cell/tissue lysates. Otherwise, select a cell lysate from Appendix 2 and enter its name and code in Box A. Complete Box C only if you are providing a purified protein kinase. Otherwise, select a purified protein kinase from Appendix 1 and enter its name and code in Box A. Please check the appropriate tick boxes. If you need assistance completing this form, please contact a technical service representative by calling toll free in North America 1-866-KINEXUS (866-546-3987) or by email at info@kinexus.ca.

CKSP-1.0 SERVICE REQUESTED:

- **Phosphorylation of a lysate with and without an added kinase**
- **Analysis of both lysates with a phospho-antibody microarray**
- **Bioinformatic selection of the most promising substrates**
- **Validation of kinase substrate candidates by immunoblotting**

** 1000 µg protein for each cell or tissue lysate sample is required*
** ~ 10 µg of each purified, active protein kinase is requested*

KINEXUS ID NUMBER
(Bar Code Identification Number)
For Kinexus Internal Use Only.

B. CLIENT-SUPPLIED CELL/TISSUE LYSATES

Customer ID Name: _____

Enter an ID name of your choice for your reference and for use in Box A of the "Client-Supplied Non-confidential Sample Description" (CKSP-NSDF-01) and "Client-Supplied Confidential Sample Description" (CKSP-CSDF-01) forms, which must be completed and provided.

A. CELL/TISSUE LYSATE AND PURIFIED PROTEIN KINASE SELECTION:

Kinexus currently offers lysates prepared from 14 different human tumour cell lines (see Appendix 2 for names and codes) and over 360 different, purified, active and recombinant human protein kinases (see Appendix 1 for names and codes) for use with the Custom Kinase Substrate Profiling Service. Check with the Kinexus website at www.kinexus.ca for new cell lysates and kinases that will become available.

Please provide the following information for each requested analysis as a separate line below. You only need to completete the "Kinase Code" and the "Lysate Code" sections if you are using kinases and lysates, respectively, that are being sourced from Kinexus. For client supplied kinases and lysates, please give a descriptive short name that corresponds to the information you have provided on the "Client-Supplied Non-confidential Kinase Description" (CKSP-NKDF-01), "Client-Supplied Confidential Kinase Description" (CKSP-CKDF-01), "Client-Supplied Non-confidential Sample Description" (CKSP-NSDF-01), and "Client-Supplied Confidential Sample Description" (CKSP-CSDF-01) forms that are being supplied with this order.

Analysis Number	Kinase Name	Kinase Code	Lysate Name	Lysate Code
1.				
2.				
3.				
4.				
5.				
6.				
7.				

C. CLIENT-SUPPLIED PURIFIED KINASE

Customer ID Name: _____

Enter an ID name of your choice for your reference and for use in Box A of the "Client-Supplied Non-confidential Kinase Description" (CKSP-NKDF-01) and "Client-Supplied Confidential Kinase Description" (CKSP-CKDF-01) forms, which must be completed and provided.

D. PRICING FOR EACH ANALYSIS:

❑ Non-confidential,
scanned with 270+ antibodies
validated with 18 antibodies
Subtotal **$2,795 US**

❑ Confidential,
scanned with 270+ antibodies
validated with 18 antibodies
Subtotal **$4,665 US**

- Note that the costs of cell lysates and purified protein kinases are extra if these are supplied by Kinexus.

❑ Purified protein kinases from Kinexus **$200-$600 US**
(see Appendix 1)

❑ Cell lysates from Kinexus **$499 US**
(see Appendix 2)

Total pricing information should be provided with a completed Service Order Form CKSP-SOF-01 that is submitted with your order.

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

Form: CKSP-NSDF-01

KINEXUS ORDER NUMBER

CLIENT SUPPLIED NON-CONFIDENTIAL SAMPLE DESCRIPTION FORM

Subject to terms of the Kinexus Service Agreement

NAME: _____ **COMPANY/INSTITUTE:** _____

(Authorized Representative or Principal Investigator)

Non-Confidential Services Requested and Sample Details:

Please refer to the Kinex™ Sample Preparation Protocol for details on preparing your samples. Clients are required to complete all Sections A-K to qualify for the non-confidential pricing level for the Kinexus Custom Kinase Substrate Profiling (CKSP) Service if they provide their own lysates for analysis. If sample details are to remain confidential, please complete instead the "Client Supplied Confidential Sample Description Form" (CKSP-CSDF-01) in Sections A-C. If you need assistance completing this form, please contact a technical service representative by calling toll free in North America 1-866-KINEXUS (866-546-3987) or by email at info@kinexus.ca. Please check the appropriate tick boxes.

A. CLIENT SCREEN ID NAME + KINEXUS SCREEN NAME:

CLIENT ID: _____ KINEXUS SCREEN: CKSP-1.0

Use the Client ID Name that you entered in Box B on the Custom Kinase Substrate Profiling Service Identification Form" (CKSP-SIF-01).

B. SAMPLE IDENTIFICATION:

Client Name for Sample: _____ Control: ❑ Yes ❑ No

Concentration: _____ Volume: _____

Clients must provide at least 1000 µg of protein at a concentration ≥ 2 mg/ml

C. SPECIES:

❑ Human *(Homo sapiens)* Sex: ❑ Male ❑ Female ❑ M/F pooled ❑ Unknown

❑ Rat *(Rattus norvegicus)* # Animals: ____ Age: _____ Weight: _____

❑ Mouse *(Mus musculus)*

❑ Other – *Provide scientific & common name:* _____

KINEXUS ID NUMBER (FOR INTERNAL USE ONLY)

(Bar Code Identification Number)

D. SAMPLE SOURCE:

Tissues: ❑ Yes ❑ No *If yes, proceed to Section E*

Cells: ❑ Yes ❑ No *If yes, proceed to Section F*

E. TISSUES:

A. Organ source of tissue: _____

B. Tissue name: _____

C. Disease condition if appropriate: _____

F. CELLS: Is your sample a primary culture? ❑ Yes ❑ No

Is your sample an established cell line? ❑ Yes ❑ No

A. Name of cell line: _____

B. Organ source of cells: _____

C. Tissue or cell type: _____

D. Disease condition if appropriate: _____

G. CELL STATE: ❑ N/A

❑ Subconfluent ❑ Quiescent

❑ Confluent ❑ Scenescent

❑ Proliferating ❑ Apoptosing

❑ Differentiated ❑ Stressed

H. FRACTIONATION:

❑ Detergent-solubilized total lysate

❑ Cytosolic (Soluble)

❑ Particulate (Detergent-solubilized)

❑ IP - *If yes, indicate antibody or ligand used:* _____

❑ Other purification: _____

I. PERTURBATION:

❑ Normal untreated *If yes, proceed to Section K*

❑ Normal treated *If yes, proceed to Section J*

❑ Diseased untreated *If yes, proceed to Section K*

❑ Diseased treated *If yes, proceed to Section J*

J. TREATMENTS: ***Please indicated if you used combined [CMB] or sequential [SEQ] treatments and provide details on your treatment:***

1. Name of compound/stimuli: _____ Concentration: _____ Time: _____ ❑ CMB ❑ SEQ

2. Name of compound/stimuli: _____ Concentration: _____ Time: _____ ❑ CMB ❑ SEQ

3. Name of compound/stimuli: _____ Concentration: _____ Time: _____ ❑ CMB ❑ SEQ

Details of treatment: _____

K. ADDITIONAL SAMPLE INFORMATION: ***Please include any additional information that differentiates your samples:***

Transgenic: ❑ Yes ❑ No Knockout: ❑ Yes ❑ No Wildtype: ❑ Yes ❑ No Transfected/Over-expressed: ❑ Yes ❑ No Mutant: ❑ Yes ❑ No

If you answered yes to any of the above, please specify details including if there was any deprivation (such as serum/growth factor/drug/site of mutation) prior to treatment:

I hereby certify that all the sample information provided in this order is correct and accurate to the best of my knowledge. To qualify for the non-confidential pricing level, I agree that all Sections A-K must be completed in full otherwise the confidential pricing level will be applied. I further acknowledge that I may be contacted by a Kinexus representative for additional information if any section is unclear.

_____ _____ _____

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

Form: CKSP-CSDF-01

KINEXUS ORDER NUMBER

CLIENT SUPPLIED
CONFIDENTIAL SAMPLE DESCRIPTION FORM

Subject to terms of the Kinexus Service Agreement

NAME: _____ **COMPANY/INSTITUTE:** _____

(Authorized Representative or Principal Investigator)

Confidential Service Requested and Sample Details:

Please refer to the "Kinex™ Sample Preparation Protocol" for details on preparing your samples. Clients are required to complete Sections A-C for the confidential pricing level for the Kinexus Custom Kinase Substrate Profiling (CKSP) Service if they provide their own lysates for analysis. Note that a confidential analysis is performed at a higher pricing level than a non-confidential analysis. Clients should instead complete all of Sections A-C on the "Client Supplied Non-Confidential Sample Description Form" (CKSP-NSDF-01) to qualify for the non-confidential pricing. If you need assistance completing this form, please contact a technical service representative by calling toll free in North America 1-866-KINEXUS (866-546-3987) or by email at info@kinexus.ca. Please check the appropriate tick boxes.

A. CLIENT SCREEN ID NAME + KINEXUS SCREEN NAME:

CLIENT ID: _____ KINEXUS SCREEN: CKSP-1.0

Use the Client ID Name that you entered in Box B on the Custom Kinase Substrate Profiling Service Identification Form" (CKSP-SIF-01).

B. SAMPLE IDENTIFICATION:

Client Name for Sample: _____ Control: ❑ Yes ❑ No

Concentration: _____ Volume: _____

Clients must provide at least 1000 µg of protein at a concentration ≥ 2 mg/ml

C. SPECIES:

❑ Human *(Homo sapiens)* Sex: ❑ Male ❑ Female ❑ M/F pooled ❑ Unknown

❑ Rat *(Rattus norvegicus)* # Animals: ____ Age: _____ Weight: _____

❑ Mouse *(Mus musculus)*

❑ Other – *Provide scientific & common name:* _____

KINEXUS ID NUMBER (FOR INTERNAL USE ONLY)

(Bar Code Identification Number)

A. CLIENT SCREEN ID NAME + KINEXUS SCREEN NAME:

CLIENT ID: _____ KINEXUS SCREEN: CKSP-1.0

Use the Client ID Name that you entered in Box A on the Custom Kinase Substrate Profiling Service Identification Form" (CKSP-SIF-01).

B. SAMPLE IDENTIFICATION:

Client Name for Sample: _____ Control: ❑ Yes ❑ No

Concentration: _____ Volume: _____

Clients must provide at least 1000 µg of protein at a concentration ≥ 2 mg/ml

C. SPECIES:

❑ Human *(Homo sapiens)* Sex: ❑ Male ❑ Female ❑ M/F pooled ❑ Unknown

❑ Rat *(Rattus norvegicus)* # Animals: ____ Age: _____ Weight: _____

❑ Mouse *(Mus musculus)*

❑ Other – *Provide scientific & common name:* _____

KINEXUS ID NUMBER (FOR INTERNAL USE ONLY)

(Bar Code Identification Number)

A. CLIENT SCREEN ID NAME + KINEXUS SCREEN NAME:

CLIENT ID: _____ KINEXUS SCREEN: CKSP-1.0

Use the Client ID Name that you entered in Box A on the Custom Kinase Substrate Profiling Service Identification Form" (CKSP-SIF-01).

B. SAMPLE IDENTIFICATION:

Client Name for Sample: _____ Control: ❑ Yes ❑ No

Concentration: _____ Volume: _____

Clients must provide at least 1000 µg of protein at a concentration ≥ 2 mg/ml

C. SPECIES:

❑ Human *(Homo sapiens)* Sex: ❑ Male ❑ Female ❑ M/F pooled ❑ Unknown

❑ Rat *(Rattus norvegicus)* # Animals: ____ Age: _____ Weight: _____

❑ Mouse *(Mus musculus)*

❑ Other – *Provide scientific & common name:* _____

KINEXUS ID NUMBER (FOR INTERNAL USE ONLY)

(Bar Code Identification Number)

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

_____ _____ _____

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

KINEXUS

Form: CKSP-NKDF-01

CLIENT-SUPPLIED NON-CONFIDENTIAL KINASE DESCRIPTION FORM

Subject to terms of the Kinexus Service Agreement

KINEXUS ORDER NUMBER

NAME: _____ **COMPANY/INSTITUTE:** _____

(Authorized Representative or Principal Investigator)

CUSTOM KINASE SUBSTRATE PROFILING SERVICE REQUESTED: (WITH CLIENT SUPPLIED KINASE)

Clients have the option of using their own purified protein kinases for the Custom Kinase Substrate Profiling analysis with non-confidential pricing if they fully describe the name, purity and source of the kinase (including full name, Swiss-Prot ID number, the animal species for which the amino acid sequence of the kinases is from, the species that the kinase was expressed in if it is recombinant, and the vender's name and catalogue number if it is commercially sourced). Please note that in the event that clients do not wish to disclose the source or nature of the antibodies that they are providing, then Confidential Pricing must apply and they must complete a CKSP-CKDF-1 form instead. Please check the appropriate tick boxes.

A. CLIENT SCREEN ID NAME:

Client ID: _____

Use the Client Screen ID Name that you entered in Box C on the "Custom Kinase Substrate Profiling Identification Form" (CKSP-SIF-01)

Clients should provide at least enough active kinase for making at least 800 µl of assay solution at the desired final concentration

B. KINASE IDENTIFICATION:

Client Name for Kinase: _____

Concentration: _____ Volume: _____

Recommended dilution for enzyme assay: _____

C. KINASE DESCRIPTION:

Kinase name: _____

SwissProt or UniProt ID number: _____

Species of origin: (based on amino acid sequence):

❑ Human ❑ Cow ❑ Rat

❑ Mouse ❑ Rabbit ❑ Other – *Provide name:* _____

Purity Description: _____

KINEXUS ID NUMBER (FOR INTERNAL USE ONLY)

(Bar Code Identification Number)

D. COMMERCIAL SOURCE OF KINASE: (if applicable)

Supplier Name: _____

Supplier Catalog Number: _____

Supplier Lot Number: _____

E. RECOMBINANT KINASE INFORMATION: (if applicable)

Species for expression: _____

Mutation or tagging: _____

F. SPECIAL INSTRUCTIONS – Handling and assay of kinase:

_____

_____

A. CLIENT SCREEN ID NAME:

Client ID: _____

Use the Client Screen ID Name that you entered in Box C on the "Custom Kinase Substrate Profiling Identification Form" (CKSP-SIF-01)

Clients should provide at least enough active kinase for making at least 800 µl of assay solution at the desired final concentration

B. KINASE IDENTIFICATION:

Client Name for Kinase: _____

Concentration: _____ Volume: _____

Recommended dilution for enzyme assay: _____

C. KINASE DESCRIPTION:

Kinase name: _____

SwissProt or UniProt ID number: _____

Species of origin: (based on amino acid sequence):

❑ Human ❑ Cow ❑ Rat

❑ Mouse ❑ Rabbit ❑ Other – *Provide name:* _____

Purity Description: _____

KINEXUS ID NUMBER (FOR INTERNAL USE ONLY)

(Bar Code Identification Number)

D. COMMERCIAL SOURCE OF KINASE: (if applicable)

Supplier Name: _____

Supplier Catalog Number: _____

Supplier Lot Number: _____

E. RECOMBINANT KINASE INFORMATION: (if applicable)

Species for expression: _____

Mutation or tagging: _____

F. SPECIAL INSTRUCTIONS – Handling and assay of kinase:

_____

_____

I hereby certify that all of the information about cell/tissue samples and kinases that I provided in this order is correct and accurate to the best of my knowledge.

_____ _____ _____

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

KINEXUS

CLIENT-SUPPLIED CONFIDENTIAL KINASE DESCRIPTION FORM

Subject to terms of the Kinexus Service Agreement

Form: CKSP-CKDF-01

KINEXUS ORDER NUMBER

NAME: _____ **COMPANY/INSTITUTE:** _____

(Authorized Representative or Principal Investigator)

CUSTOM KINASE SUBSTRATE PROFILING SERVICE REQUESTED: (WITH CLIENT SUPPLIED KINASE)

Clients have the option of using their own purified protein kinases for the Custom Kinase Substrate Profiling analysis at a substantial discount if they fully describe the name, purity and source of the kinase (including full name, Swiss-Prot ID number, the animal species for which the kinase is from, the species that the kinase was expressed in if it is recombinant, and the vender's name and catalogue number if it is commercially sourced). In this event, clients should instead complete a CKSP-NKDF-1 form. This form applies in the event that clients do not wish to disclose the source or nature of the kinases that they are providing, and Confidential Pricing must apply. Please check the appropriate tick boxes.

A. CLIENT SCREEN ID NAME:

CLIENT ID: _____

Use the Client Screen ID Name that you entered in Box C on the "Custom Kinase Substrate Profiling Identification Form" (CKSP-SIF-01)

B. KINASE IDENTIFICATION:

Client Name for Kinase: _____

Concentration: _____ Volume: _____

Recommended dilution for enzyme assay: _____

Clients should provide at least enough active kinase for making at least 800 µl of assay solution at the desired final concentration.

C. SPECIES OF KINASE ORIGIN: (based on amino acid sequence)

- ❑ Human
- ❑ Cow
- ❑ Mouse
- ❑ Rabbit
- ❑ Rat
- ❑ Other – *Provide common name:* _____

Purity Description: _____

KINEXUS ID NUMBER (FOR INTERNAL USE ONLY)

(Bar Code Identification Number)

D. SPECIAL INSTRUCTIONS FOR HANDLING AND ASSAY OF KINASE:

_____

_____

A. CLIENT SCREEN ID NAME:

CLIENT ID: _____

Use the Client Screen ID Name that you entered in Box C on the "Custom Kinase Substrate Profiling Identification Form" (CKSP-SIF-01)

B. KINASE IDENTIFICATION:

Client Name for Kinase: _____

Concentration: _____ Volume: _____

Recommended dilution for enzyme assay: _____

Clients should provide at least enough active kinase for making at least 800 µl of assay solution at the desired final concentration.

C. SPECIES OF KINASE ORIGIN: (based on amino acid sequence)

- ❑ Human
- ❑ Cow
- ❑ Mouse
- ❑ Rabbit
- ❑ Rat
- ❑ Other – *Provide common name:* _____

Purity Description: _____

KINEXUS ID NUMBER (FOR INTERNAL USE ONLY)

(Bar Code Identification Number)

D. SPECIAL INSTRUCTIONS FOR HANDLING AND ASSAY OF KINASE:

_____

_____

I hereby certify that all of the information about cell/tissue samples and kinases that I provided in this order is correct and accurate to the best of my knowledge.

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

COMMERCIAL INVOICE

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

NO. OF PKGS	TYPE OF PACKAGING	QUANTITY OF SAMPLES	COMPLETE AND ACCURATE COMMODITY DESCRIPTION	UNIT VALUE
	__ FedEx Letter __ FedEx Pak __ Box __ Other	*Total number of 1.5 ml Eppendorf tubes:*	Non hazardous, non infectious protein for research and development diagnostic purposes. Samples are not for resale and there is no commercial value. Samples are packaged on Dry Ice, Class 9, UN 1845, Group 3 (____ X ____ kgs).	$1.00 *per sample*

TOTAL NO. OF PACKAGES	TOTAL WEIGHT OF PACKAGES	TOTAL DECLARED VALUE
		$

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

SIGNATURE AND STATUS OF AUTHORIZED PERSON

_____ _____

Print Name *Title*

_____ _____

Authorized Signature *Date (month/day/year)*

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

PROTEOMICS SERVICES AGREEMENT

SERVICE AGREEMENT NO.

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

_____

_____

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: _____

Supplemental Data

Additional Examples of Custom Kinase Substrate Profiling

The table below provides the results of Kinex™ Antibody Microarray analysis with the cAMP-dependent Protein Kinase (PKA) and Src, which are known protein-serine/threonine and protein-tyrosine kinases, respectively. Note that many of the phospho-serine and phospho-threonine-specific antibodies revealed increased phosphorylation by the Src protein-tyrosine kinase. This may have been due to cross-reactivities with these antibodies with actual tyrosine-phosphorylated sites or secondary phosphorylations due to the activation of protein-serine/threonine kinases by their tyrosine phosphorylation by Src.

Site Type	STY	STY	STY	ST	ST	ST	Y	Y	Y
%CFC	No. P-Ab ≥25	No. P-Ab ≥50	No. P-Ab ≥100	No. P-Ab ≥25	No. P-Ab ≥50	No. P-Ab ≥100	No. P-Ab ≥25	No. P-Ab ≥50	No. P-Ab ≥100
PKA	58	27	12	46	22	10	12	5	2
Src	61	35	9	50	26	8	11	9	1

Number of Phospho-site Antibodies Showing Increased Phosphorylation with Addition of Kinase

Table Legend - Detection of increased phosphorylation with addition of PKA and the protein-tyrosine kinase Src to HeLa cell lysates as revealed with the Kinex™ KAM-1.1 antibody microarray with 270 phospho-site antibodies (P-Ab). The percentage change from control (%CFC) with the addition of the protein kinase is shown. S,T and Y corresponds to phospho-sites antibodies developed for serine (S), threonine (T) and tyrosine (Y) phosphorylation sites.

The figure on the following page provides some of the results of CKSP analysis with either PKA or Src, where the phospho-site antibody microarray results have been validated by immunoblotting. Strong and moderate positive determinants for either PKA or Src recognition are coloured in blue and orange, respectively, in the “Sequence” column. In the Western blots shown, the phosphorylation signal in the absence of the added kinases is on the left and the phosphorylation signal in the presence of the added kinase is on the right. Detected bands correspond to the expected sizes of the target phosphoproteins. %CFC refers to the percent increased phosphorylation of the target protein by the added kinase compared with its absence as detected with the Kinex™ KAM-1.1 antibody microarray. In the case of the apparent phosphorylation of Lyn Y507 by Src, it is possible that the increased signal may be due to cross-reactivity of the added Src at its C-terminal Y530 site with the Lyn Y507 phospho-antibody.

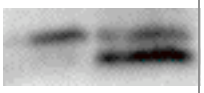
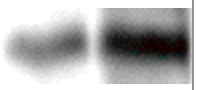
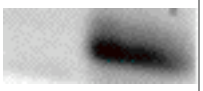
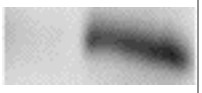
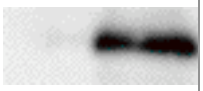
Protein Kinase	Substrate Protein	Phospho-Site	Sequence	Kinex %CFC	Western Blot
PKA	Plk1	T210	YDGERKKTLCGTPNY	93	
PKA	SOX9	S181	YQPRRRKSVKNGQAE	43	
Src	GSK3α/β	Y279/ Y216	RGEPNVSYICSRYYR	91	
Src	INSR/IGF1R	Y1189/Y1190	RDIYETDYYRKGGKG	65	
Src	Lyn	Y507	YTATEGQYQQQPXXX	82	
Src	STAT5A	Y694	LAKAVDGYVKPQIKQ	66	

Figure Legend - Immunoblotting analysis of putative PKA and Src phosphorylation sites in endogenous substrates in HeLa cell lysates. The column with the "Kinex %CFC" shows the increased phosphorylation detected on the Kinex™ KAM-1.1 microarray with the phospho-site antibody indicated upon addition of either PKA or Src to the HeLa cell lysate in the presence of ATP. With the Western blots, minus the added kinase is on the left and plus either PKA or Src is on the right. The apparent M.W. of the detected immunoreactive bands were consistent with the expected sizes of the target antigens of the phospho-site antibodies. Plk1 = Polo-like kinase –1, GSK3α/β = Glycogen Synthase Kinase 3 alpha and beta isoforms, INSR = Insulin Receptor, IGF1R = Insulin-like Growth Factor 1 Receptor.