

KINEX™ SERVICES

PROTEIN KINASE MICROARRAY CUSTOMER INFORMATION PACKAGE



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KINEXUS

TABLE OF CONTENTS

Introduction to Kinex™ Protein Kinase Microarray Services		PDF Page No.
1.	Introduction	3
2.	Kinex™ Protein Kinase Microarray-based Small Molecule Inhibitor Profiling Platform	5
3.	Layout of the Kinex™ Protein Kinase Microarray-200	7
4.	Examples of Compound Inhibition Profiling with the Kinex™ Protein Kinase Microarray-200..	12
5.	Kinase Substrate Profiling with the Kinex™ Protein Kinase Microarray-200.....	16
6.	Antibody Profiling with the Kinex™ Protein Kinase Microarray-200.....	22
7.	Detection of Recombinant Protein Binding with the Kinex™ Protein Kinase Microarray-200...	22
Service Ordering Information		
8.	Ordering information	23
8.1	Kinex™ Protein Kinase Microarray-based Small Molecule Inhibitor Profiling Service	23
8.2	Kinex™ Protein Kinase Microarray-based Kinase Substrate Profiling Service	24
8.3	Kinex™ Protein Kinase Microarray-based Protein Interaction Profiling Service	25
8.4	Turnaround Time	26
Shipping and Pricing Information		
9.	Pricing Information	26
10.	Shipping Information	26
11.	Further Information on Forms to be Completed	27
Follow Up Services		
12.	Follow Up Services	31
Appendices – Forms for Ordering		
13.	Service Order Form (KPKM-SOF)	33
14.	Service Identification Form (KPKM-SIF)	34
15.	Client-Supplied Non-Confidential Sample Description Form - Compounds (NSDF-C)	35
16.	Client-Supplied Non-Confidential Sample Description Form - Proteins/Peptides (NSDF-P)	36
17.	Client-Supplied Non-Confidential Sample Description Form - Antibodies (NSDF-AB)	37
18.	Client-Supplied Confidential Sample Description Form - Compounds (CSDF-C)	38
19.	Client-Supplied Confidential Sample Description Form - Proteins/Peptides (CSDF-P)	39
20.	Client-Supplied Confidential Sample Description Form - Antibodies (CSDF-AB)	40
21.	Commercial Invoice - Compounds - Not frozen (For customers outside of Canada)	41
22.	Commercial Invoice - Compounds - Frozen (For customers outside of Canada)	42
23.	Commercial Invoice - Proteins/Peptides - Not frozen (For customers outside of Canada)	43
24.	Commercial Invoice - Proteins/Peptides - Frozen (For customers outside of Canada)	44
25.	Kinexus Proteomics Services Agreement	45

KINEX™ KINASE MICROARRAY SERVICES

1. INTRODUCTION

The Kinex™ Protein Kinase Microarray (KPKM) services are a convenient and very cost-effective solution to assist scientists in the evaluation of a wide panel of diverse protein kinases as targets for potential kinase inhibitors, as substrates for kinases and proteases, and binding partners for proteins and peptides. These services utilize our unique protein kinase microarrays with different detection methods depending on the specific application. Any of the results from these economical and rapid approaches can be further validated with complementary methods that are available with our discovery platform of integrated proteomics services.

Protein kinases constitute the single largest mammalian enzyme family with at least 515 members in the human proteome. They have been implicated in a wide range of complex cellular functions and pathways, ranging from metabolic regulation to tumorigenesis. Since many human diseases result from over-activation of protein kinases due to mutations and/or over-expression, they have emerged as attractive targets in the search for new therapeutic agents in the pharmaceutical industry. Approximately one third of protein targets under investigation in the pharmaceutical industry are protein kinases, underscoring the promise of protein kinase inhibitors for the treatment of human diseases. We believe that within the next decade, over half of the drugs in clinical trials will be kinase inhibitors. Currently, more than a dozen of small-molecule kinase inhibitors have been approved for various disease indications (Table 1), and about 150 kinase-targeted drugs are in clinical development and many more are in various stages of pre-clinical development. Almost all of them are directed towards the adenosine triphosphate (ATP) binding site and display different selectivities, potencies and pharmacokinetic properties. Since the ATP-binding sites of protein kinases are highly conserved, the selectivity of kinase inhibitors becomes one of the most important issues in drug discovery process.

The selectivity of a kinase inhibitor was traditionally monitored only sporadically throughout the discovery process by *in vitro* kinase activity assays against a small subset of selected kinases. This appears to have contributed to the failure of many compounds during the late stage of development, and highlights the importance of comprehensive assessing of kinases-inhibitor selectivity during the early stage of drug discovery. Over the past few years, the size of the recombinant kinase panels has been increased dramatically to cover more than 300 protein kinases. Despite of the progress, it remained both technically and financially challenging to systematically assess the specificity of a compound against hundreds of kinases, as the assays are time-consuming and costly, and comprehensive knowledge of kinases and their substrates is still lacking.

Table 1. FDA approved small-molecule kinase inhibitor drugs (2009)

Name of Inhibitor	Alternative names	Company	Target
Celecoxib	Celebrex	Pfizer	PDK1
Dasatinib	BMS-354825, Sprycel	Bristol-Myers Squibb,	Abl, Arg, Kit, PDGF-beta, Src family kinases
Everolimus	RAD001, Certican	Novartis, Schering	mTOR
Fasudil	AT877, HA1077, Eiril	Asahi Chemical's	ROCK
Gleevec	Glivec, Imatinib mesylate, STI571	Novartis	Abl, Arg, PDGFR, DDR1, Kit, Lck
Iressa	Gefitinib, ZD1839	AstraZeneca	EGFR
Lapatinib	GW572016, GW2016, Tykerb	GlaxoSmithKline	EGFR, ErbB2
Nexavar	Sorafenib tosylate, BAY 43-9006	Bayer, Onyx	Raf1, Kit, VEGFR-2, VEGFR-3, PDGFR-?, Flt3, Ret, Fms
Nilotinib	AMN-107, Tassigna	Novartis	Kit, PDGFRA, Abl, Arg
Rapamune	Rapamycin, Srilimus	Wyeth	mTOR
Sutent	Sunitinib, SU11248	Pfizer, SUGEN	Kit, VEGFR, Flt3, PDGFR, Ret
Tarceva	Erlotinib, OSI-774, CP358774	Genentech, OSI Pharm., Roche	EGFR, ErbB3, VEGFR, PDGFR, Kit
Toceranib	Palladia, SU11654, Masitinib	Pfizer	Kit, VEGFR, Flt3, PDGFR
Torisel	Temsirolimus	Wyeth	mTOR
Valproate			GSK3-alpha, GSK3-beta as well as others including ITPK1

To reduce the costs of kinase inhibitor counter screens, alternative methods have been developed to identify protein kinases that are potentially affected by candidate drug compounds. Ambit Biosciences (www.kinomescan.com) developed a high-throughput method named KINOMEScan™ for screening small molecule kinase inhibitors against a panel of about 300 human kinases. It is based on a competition binding assay that quantitatively measures the ability of a compound to compete with an immobilized, active site-directed ligand to the bacterially expressed T7-phage tagged human kinases. The ability of the test compound to compete with the immobilized

ligand is measured by quantitative PCR of the T7 tags of the displaced kinases. Each kinase is assayed individually for each compound, which requires relatively larger quantities of compounds. Kinases expressed as fusion proteins in *E. coli* may not be in their native conformations due to the lack of some post-translational modifications, which could potentially impact the binding of compounds. In contrast, an *in situ* kinase profiling platform, Kinativ™, offered by ActivX Biosciences, utilizes acyl phosphate-containing nucleotide probes that react selectively and covalently at the ATP binding sites in combination with a mass spectrometry-based detection method to assay the kinase binding affinity of compounds in protein lysates where native post-translational modifications and protein-protein interactions are preserved. However, the approach suffers from a few drawbacks including interference from other nucleotide-binding proteins, and binding bias towards kinases in high-abundance.

2. KINEX™ PROTEIN KINASE MICROARRAY-BASED SMALL MOLECULE INHIBITOR PROFILING PLATFORM

Recognizing the importance of elucidating the inhibition profiles of compounds, Kinexus has developed an innovative microarray-based profiling platform for screening small-molecule protein kinase inhibitors (Figure 1). The cores of this technology consist of a protein kinase microarray and a biotinylated proprietary ATP probe developed at Kinexus. The probe has been shown to display affinity for the majority of protein kinases tested by our internal research work (see Section 3). Co-incubating a test compound with the biotinylated ATP probe on the protein kinase microarray allows simultaneous determination of the affinity of the compound against hundreds of protein kinases on the array on a competition binding basis. The kinases to which the compound exhibits binding will experience a reduction of the binding of the ATP probe, and the remaining ATP probe covalently bound to the kinases on the array can be detected with the fluorescently-labeled streptavidin conjugates. Compared to the aforementioned KINOMEscan™ and Kinativ™, advantages of our microarray-based inhibitor profiling platform include higher throughput, small amounts of compound required, and the use of active protein kinases expressed in eukaryotes. Without the requirements for any sophisticated analytical instrument such as quantitative PCRs and mass spectrometers, our technology presents a quick and effective approach to survey a broad spectrum of the human kinome for compound inhibition profiling prior to any in-depth assays to be performed. Thus, the protein kinase microarray-based inhibitor profiling complements well with our existing Kinase Inhibitor Profiling services that are based on measurement of phosphotransferase activity. Any hits from the Kinex™ Kinase Microarray can be confirmed with our Kinase Inhibitor Profiling services against the very same preparations of protein kinases.

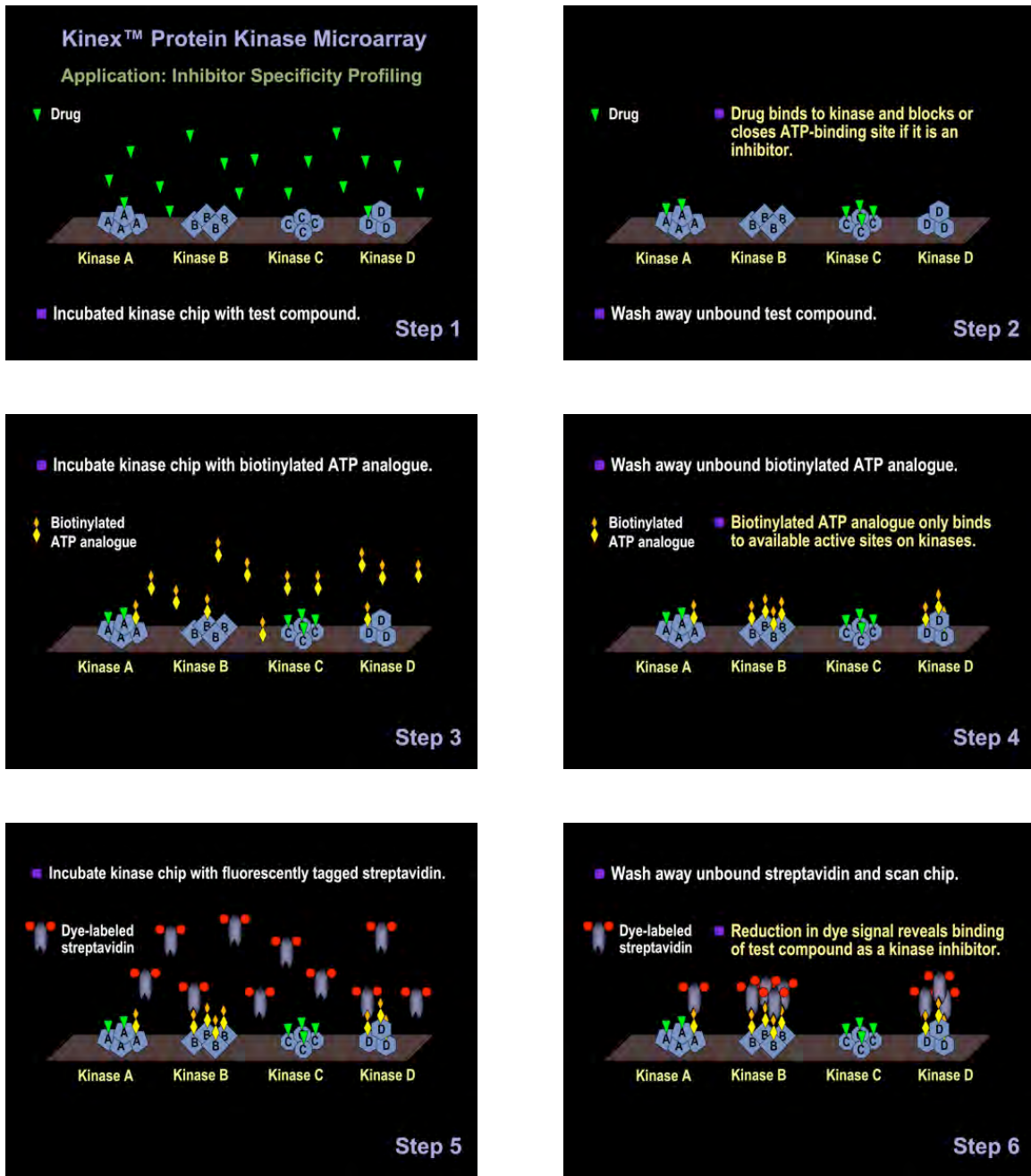


Figure 1. Schematic depiction of Protein Kinase Microarray-based small molecule inhibitor profiling platform.

3. LAYOUT OF THE KINEX™ PROTEIN KINASE MICROARRAY 200

The first generation Kinex™ Protein Kinase Microarray-200 features 200 active recombinant human protein kinases originally expressed in an insect expression system. Each array consists of 3 identical fields to allow 3 assays with either 2 different compounds at single concentrations and a control set without any compounds or a single compound of 3 different concentrations to be carried out simultaneously, with one field reserved for the probe-only control. Each kinase is spotted in triplicate within a field on a glass slide (Figure 2). In addition, multiple internal control samples have been incorporated onto the arrays during the array printing process for quality control purpose.

1	1	1	2	2	2	3	3	3	4	4	4	5	5	5	6	6	6	7	7	7	8	8	8	9	9	9
10	10	10	11	11	11	12	12	12	13	13	13	14	14	14	15	15	15	16	16	16	17	17	17	18	18	18
19	19	19	20	20	20	21	21	21	22	22	22	23	23	23	24	24	24	25	25	25	26	26	26	27	27	27
28	28	28	29	29	29	30	30	30	31	31	31	32	32	32	33	33	33	34	34	34	35	35	35	36	36	36
37	37	37	38	38	38	39	39	39	40	40	40	41	41	41	42	42	42	43	43	43	44	44	44	45	45	45
46	46	46	47	47	47	48	48	48	49	49	49	50	50	50	51	51	51	52	52	52	53	53	53	54	54	54
55	55	55	56	56	56	57	57	57	58	58	58	59	59	59	60	60	60	61	61	61	62	62	62	63	63	63
64	64	64	65	65	65	66	66	66	67	67	67	68	68	68	69	69	69	70	70	70	71	71	71	72	72	72
73	73	73	74	74	74	75	75	75	76	76	76	77	77	77	78	78	78	79	79	79	80	80	80	81	81	81
82	82	82	83	83	83	84	84	84	85	85	85	86	86	86	87	87	87	88	88	88	89	89	89	90	90	90
91	91	91	92	92	92	93	93	93	94	94	94	95	95	95	96	96	96	97	97	97	98	98	98	99	99	99
100	100	100	101	101	101	102	102	102	103	103	103	104	104	104	105	105	105	106	106	106	107	107	107	108	108	108
109	109	109	110	110	110	111	111	111	112	112	112	113	113	113	114	114	114	115	115	115	116	116	116	117	117	117
118	118	118	119	119	119	120	120	120	121	121	121	122	122	122	123	123	123	124	124	124	125	125	125	126	126	126
127	127	127	128	128	128	129	129	129	130	130	130	131	131	131	132	132	132	133	133	133	134	134	134	135	135	135
136	136	136	137	137	137	138	138	138	139	139	139	140	140	140	141	141	141	142	142	142	143	143	143	144	144	144
145	145	145	146	146	146	147	147	147	148	148	148	149	149	149	150	150	150	151	151	151	152	152	152	153	153	153
154	154	154	155	155	155	156	156	156	157	157	157	158	158	158	159	159	159	160	160	160	161	161	161	162	162	162
163	163	163	164	164	164	165	165	165	166	166	166	167	167	167	168	168	168	169	169	169	170	170	170	171	171	171
172	172	172	173	173	173	174	174	174	175	175	175	176	176	176	177	177	177	178	178	178	179	179	179	180	180	180
181	181	181	182	182	182	183	183	183	184	184	184	185	185	185	186	186	186	187	187	187	188	188	188	189	189	189
190	190	190	191	191	191	192	192	192	193	193	193	194	194	194	195	195	195	196	196	196	197	197	197	198	198	198
199	199	199	200	200	200																					

Figure 2. Layout of the protein kinases on the Kinex™ Protein Kinase Microarray-200 and one of three grids available on the chip. Positions of control spots are not indicated. Refer to Table 2A for the identities of the protein kinases in each spot position.

Table 2A. Listing of protein kinases on the Kinex™ Protein Kinase Microarray-200

Number	Protein Kinase	Group	Family
1	MRCK-alpha	AGC	DMPK
2	ROCK1	AGC	DMPK
3	ROCK2	AGC	DMPK
4	DMPK	AGC	DMPK
5	MRCK-beta	AGC	DMPK
6	GRK5	AGC	GRK
7	PKAc-alpha (his-tag)	AGC	PKA
8	PKAc-beta	AGC	PKA
9	PKAc-gamma	AGC	PKA
10	PDK1	AGC	PKB
11	AKT1	AGC	PKB
12	AKT2 (his-tag)	AGC	PKB
13	AKT3	AGC	PKB
14	AKT2	AGC	PKB
15	PKC-theta	AGC	PKC
16	PKC-iota	AGC	PKC
17	PKC-nu	AGC	PKC
18	PKC-beta I	AGC	PKC
19	PKC-beta II	AGC	PKC
20	PKC-epsilon	AGC	PKC
21	PKC-zeta	AGC	PKC
22	PKC-delta	AGC	PKC
23	PKC-eta	AGC	PKC
24	PKC-gamma	AGC	PKC
25	PKC-alpha (Xenopus)	AGC	PKC
26	PRKG1(PKG1)	AGC	PKG
27	p70S6K-beta	AGC	RSK
28	RSK1	AGC	RSK
29	RSK3	AGC	RSK
30	RSK4	AGC	RSK
31	RSK2	AGC	RSK
32	MSK1	AGC	RSK
33	p70S6K	AGC	RSK
34	SGK2	AGC	SGK
35	SGK3	AGC	SGK
36	SGK1	AGC	SGK
37	CAMK1	CAMK	CaMK1
38	CAMK1-gamma	CAMK	CAMK1
39	CAMK4	CAMK	CAMK1
40	CAMK1-delta	CAMK	CAMK1
41	CAMK1-beta	CAMK	CAMK1
42	CAMK2-alpha	CAMK	CaMK2
43	CAMK2D	CAMK	CAMK2
44	CAMK2-gamma	CAMK	CAMK2
45	CAMK2-beta	CAMK	CaMK3
46	PASK	CAMK	CAMKL
47	MARK1	CAMK	CAMKL
48	MARK3	CAMK	CAMKL
49	CHK1	CAMK	CAMKL
50	AMPKA1B1G1	CAMK	CAMKL

Number	Protein Kinase	Group	Family
51	AMPKA2B1G1	CAMK	CAMKL
52	DAPK3	CAMK	DAPK
53	DAPK1	CAMK	DAPK
54	DCAMKL2	CAMK	DCAMKL
55	MAPKAPK2	CAMK	MAPKAPK
56	MAPKAPK3	CAMK	MAPKAPK
57	MLCK	CAMK	MLCK
58	MYLK2	CAMK	MLCK
59	MYLK3	CAMK	MLCK
60	MNK2	CAMK	MNK
61	PIM1	CAMK	PIM
62	PIM2	CAMK	PIM
63	PKC-mu	CAMK	PKD
64	PKD2	CAMK	PKD
65	CHK2	CAMK	RAD53
66	TSSK2	CAMK	TSSK
67	CDK1/CCNA2	CMGC	CDK
68	CDK2/CCNE1	CMGC	CDK
69	CDK7/CCNH/MNAT1	CMGC	CDK
70	CDK9/CCNK	CMGC	CDK
71	CDK2/CCNA2	CMGC	CDK
72	CDK4/CCND1	CMGC	CDK
73	CDK5/p25	CMGC	CDK
74	CDK6/CCND1	CMGC	CDK
75	CDK6/CCND3	CMGC	CDK
76	CDK3/CCNE1	CMGC	CDK
77	CDK4/CCND3	CMGC	CDK
78	CLK1	CMGC	CLK
79	CLK2	CMGC	CLK
80	CLK3	CMGC	CLK
81	HIPK1	CMGC	Dyrk
82	HIPK3	CMGC	Dyrk
83	HIPK4	CMGC	Dyrk
84	GSK3-alpha	CMGC	GSK
85	GSK3-beta	CMGC	GSK
86	JNK1	CMGC	MAPK
87	ERK2	CMGC	MAPK
88	p38-beta	CMGC	MAPK
89	p38-delta	CMGC	MAPK
90	p38-gamma	CMGC	MAPK
91	ERK1	CMGC	MAPK
92	p38-alpha	CMGC	MAPK
93	MSSK1	CMGC	SRPK
94	SRPK1	CMGC	SRPK
95	SRPK2	CMGC	SRPK
96	PI3KCB/p85-alpha	Lipid kinase	
97	PI3KCA/p85-alpha	Lipid kinase	
98	AuroraC	Other	AUR
99	AuroraB	Other	AUR
100	AuroraA (his-tag)	Other	AUR

Table 2B. Listing of protein kinases on the Kinex™ Protein Kinase Microarray-200

Number	Protein Kinase	Group	Family
101	CAMKK1	Other	CAMKK
102	CAMKK2	Other	CAMKK
103	CK2-alpha1	Other	CK2
104	TBK1	Other	IKK
105	NEK7	Other	NEK
106	NEK2	Other	NEK
107	NEK6	Other	NEK
108	PKR	Other	PEK
109	PLK1	Other	PLK
110	TOPK	Other	TOPK
111	MEKK2	STE	STE11
112	MEKK3	STE	STE11
113	ASK1	STE	STE11
114	KHS1	STE	STE20
115	MST1	STE	STE20
116	PAK4	STE	STE20
117	TAOK2	STE	STE20
118	PAK1/CDC42	STE	STE20
119	PAK3	STE	STE20
120	MINK1	STE	STE20
121	MST3	STE	STE20
122	LOK	STE	STE20
123	MYO3-beta	STE	STE20
124	TAOK1	STE	STE20
125	STK3 (MST2)	STE	STE20
126	MST4	STE	STE20
127	PAK7 (PAK5)	STE	STE20
128	MEK1	STE	STE7
129	MEK2	STE	STE7
130	COT	STE	STE-Unique
131	ABL2	TK	ABL
132	ABL1 (his-tag)	TK	ABL
133	MER	TK	Axl
134	TYRO3	TK	Axl
135	AXL	TK	Axl
136	CSK	TK	CSK
137	CSK	TK	CSK
138	DDR2	TK	DDR
139	HER2	TK	EGFR
140	HER4	TK	EGFR
141	EPHA1	TK	EPH
142	EPHA2	TK	EPH
143	EPHA3	TK	EPH
144	EPHA4	TK	EPH
145	EPHB1	TK	EPH
146	EPHB4	TK	EPH
147	EPHB3	TK	Eph
148	EPHB2	TK	Eph
149	FAK	TK	FAK
150	PYK2 (FAK2)	TK	FAK

Number	Protein Kinase	Group	Family
151	FER	TK	Fer
152	FES	TK	Fer
153	FGFR1 (FLT2)	TK	FGFR
154	FGFR3	TK	FGFR
155	IGF1R	TK	InsR
156	IRR	TK	InsR
157	InsR	TK	InsR
158	JAK2	TK	JAK
159	MET (956-end his-tag)	TK	MET
160	RON	TK	MET
161	MET	TK	Met
162	MUSK	TK	MUSK
163	FMS	TK	PDGFR
164	KIT	TK	PDGFR
165	FLT3	TK	PDGFR
166	PDGFR-beta	TK	PDGFR
167	PDGFR-alpha	TK	PDGFR
168	RET	TK	RET
169	ROR2	TK	ROR
170	FYNA	TK	Src
171	LYNA	TK	Src
172	SRC	TK	Src
173	BLK	TK	Src
174	FRK	TK	Src
175	FGR	TK	Src
176	HCK	TK	Src
177	BRK	TK	Src
178	LCK	TK	Src
179	SYK	TK	SYK
180	ZAP70	TK	Syk
181	ITK	TK	Tec
182	TXK	TK	Tec
183	BTK	TK	Tec
184	BMX	TK	Tec
185	TEK	TK	TIE
186	TRKC	TK	Trk
187	TRKA	TK	Trk
188	TRKB	TK	Trk
189	FLT1 (VEGFR1)	TK	VEGFR
190	KDR (VEGFR2)	TK	VEGFR
191	LYN B	TK	Src
192	IRAK2	TKL	IRAK
193	IRAK4	TKL	IRAK
194	B-RAF	TKL	RAF
195	RAF1(EE)	TKL	RAF
196	RIPK2	TKL	RIPK
197	ALK4	TKL	STKR
198	TGFBR2	TKL	STKR
199	ALK1	TKL	STKR
200	ALK2	TKL	STKR

The 200 protein kinases spotted on the arrays cover most of the major groups of the human kinome and respective families (Table 2). We expect to enhance the coverage once more active kinases become available to us in the near future. Thus far, the vast majority of the 200 kinases tested have shown affinity for our proprietary ATP analogue probe (Table 3). Relative affinities of specific protein kinases for the ATP analogue probe are summarized in Table 4. Those kinases that display the strongest ATP analogue probe binding will yield the most reliable inhibitor screening results. Note that the ATP analogue probe is also useful for the detection of protein kinase activators as they may improve the binding of the ATP analogue probe. Therefore, it should be feasible to detect protein kinase activation as a consequence of phosphorylation *in vitro* on the chip by an added protein kinase or partial proteolysis by a protease that relieves inhibition by non-catalytic domains.

Table 3. Affinity of the ATP analogue probe for various protein kinase classes on the Kinex™ Protein Kinase Microarray – 200.

Kinase Group	No. of Kinases	% of Different Kinases Labeled by the Probe
AGC	36	69.4
CAMK	30	73.3
CMGC	29	75.9
STE	20	65
TK	61	52.5
TKL	9	77.8
Other+Lipid Kinase	15	73.3

Table 4. Relative affinity of the ATP analogue probe for various protein kinase classes on the Kinex™ Protein Kinase Microarray – 200.

CAMK Group	ATP Binding	CMGC Group	ATP Binding	TK Group	ATP Binding	TK Group	ATP Binding
CAMK1-delta	+++	CDK2/CCNA2	+++	ZAP70	+++	FYNA	-
CHK1	+++	SRPK1	+++	ABL2	+++	LYN B	-
CAMK2a	+++	CDK4/CCND3	+++	AXL	+++	ITK	-
PKCmu	+++	GSK3-beta	+++	TXK	+++	FMS	-
MARK3	+++	p38-alpha	+++	BTK	+++	SRC	-
DAPK3	+++	CDK7/CCNH	+++	KIT	+++	EPHA4	-
CAMK1-beta	+++	CDK9/CCNK	+++	FGFR1 (FLT2)	+++		
MNK2	+++	GSK3-alpha	+++	FER	+++	AGC Group	ATP Binding
TSSK2	+++	HIPK4	+++	TYRO3	+++	GRK5	+++
PKD2	+++	CDK6/CCND3	+++	RET	+++	PKC-iota	+++
CAMK2-beta	+++	MSSK1	++	ROR2	+++	PKC-theta	+++
AMPKA1B1G1	+++	CDK4/CCND1	++	TRKC	+++	p70S6K	+++
AMPKA2B1G1	++	CDK6/CCND1	++	TEK	+++	PKC-nu	+++
PIM2	++	ERK2	++	IGF1R	+++	PKC-delta	+++
CAMK1-gamma	++	CLK3	++	ABL1	+++	PKC-epsilon	+++
MAPKAPK3	++	CDK3/CCNE1	+	FLT1 (VEGFR1)	+++	PKC-zeta	+++
CAMK2-gamma	++	CLK2	+	IRR	+++	PKC-beta II	+++
PIM1	++	JNK1	+	BMX	+++	PKAc-alpha	+++
MAPKAPK2	++	SRPK2	+	JAK2	++	PKAc-beta	+++
MARK1	+	CLK1	+	EPHA1	++	AKT2	++
DCAMKL2	+	ERK1	+	MUSK	++	MRCK-alpha	++
DAPK1	+	CDK2/CCNE1	+	TRKA	++	PDK1	++
MLCK	-	HIPK3	-	FGFR3	++	p70S6K-beta	++
MYLK3	-	p38-beta	-	PDGFRA	++	PKC-eta	++
CAMK4	-	CDK1/CCNA2	-	FGR	++	RSK2	++
CHK2	-	p38-gamma	-	LYNA	+	MRCK-beta	++
PASK	-	p38-delta	-	BLK	+	AKT2	+
MYLK2	-	HIPK1	-	EPHA2	+	RSK3	+
CAMK1	-	CDK5/p25	-	DDR2	+	PKC-gamma	+
CAMK2-delta	-			TRKB	+	MSK1	+
		STE Group	ATP Binding	EPHB4	+	ROCK1	+
		PAK4	+++	HCK	+	DMPK	+
		COT	+++	HER2	-	SGK3	+
		TAOK2	++	PDGFRB	-	PKAc-gamma	-
		PAK3	++	MET	-	SGK2	-
		MEKK2	++	HER4	-	ROCK2	-
		PAK7 (PAK5)	++	InsR	-	RSK1	-
		MEK1	++	EPHB1	-	AKT3	-
		KHS1	++	EPHA3	-	RSK4	-
		PAK1/CDC42	++	RON	-	AKT1	-
		TAOK1	++	MET	-	SGK1	-
		MINK1	+	FES	-	PRKG1 (PKG1)	-
		MEK2	+	FAK	-	PKC-alpha	-
		LOK	+	PYK2 (FAK2)	-	PKC-beta I	-
		MYO3b	-	LCK	-		
		STK3 (MST2)	-	FRK	-	TLK Group	ATP Binding
		MEKK3	-	KD (VEGFR2)	-	TGFBR2	+++
		MST4	-	CSK	-	ALK4	+++
		MST3	-	FLT3	-	RAF1(EF)	+++
		ASK1	-	SYK	-	B-RAF	+++
		MST1	-	CSK	-	RIPK2	++
				EPHB2	-	ALK2	+
				MER	-	IRAK2	+
				EPHB3	-	IRAK4	-
				BRK	-	ALK1	-

4. EXAMPLES OF COMPOUND INHIBITION PROFILING WITH THE KINEX™ PROTEIN KINASE MICROARRAY - 200

The following figures provide examples of the performance of the Kinex™ Protein Kinase Microarray – 200 for monitoring the inhibitory activity of selected compounds on the binding of our ATP analogue probe to various protein kinases on the chip. Staurosporine is an alkaloid that is known to inhibit a wide spectrum of protein kinases (Figure 4). In Figure 4A, we present an image of the scanned chip following preincubations without and with staurosporine. The strong spot signals correspond to the binding of the ATP analogue probe. In Figure 4B and C, we have shown those protein kinases within specific classes that demonstrated the highest degree of inhibition by the added staurosporine. In Figure 5, we identify those protein kinases that revealed the largest inhibitions of ATP analogue probe binding by SB203580 and SB220025, which are commonly used inhibitors of the p38 MAP kinases. Only 30 of the protein kinases tested exhibited 25% or greater inhibition with 5 μM concentrations of SB203580 or SB220025. In Figure 6, we show the effects of olomoucine and alsterpauillone, which are known inhibitors of cyclin-dependent protein kinases, on all of the CMGC Family protein kinases on the Kinex™ Protein Kinase Microarray-200 with respect to the binding of our ATP analogue probe.

Signal intensity for ATP probe binding on the Kinex™ Protein Kinase Microarray–200.

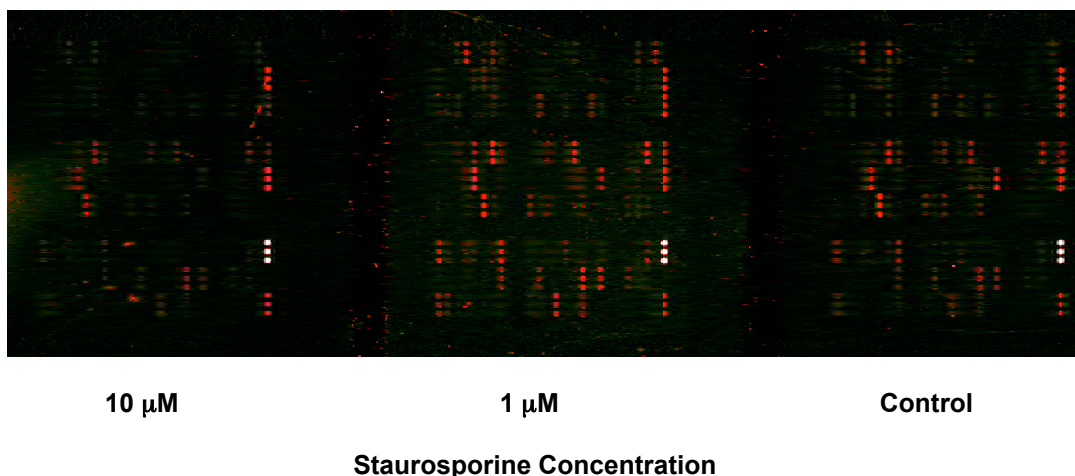
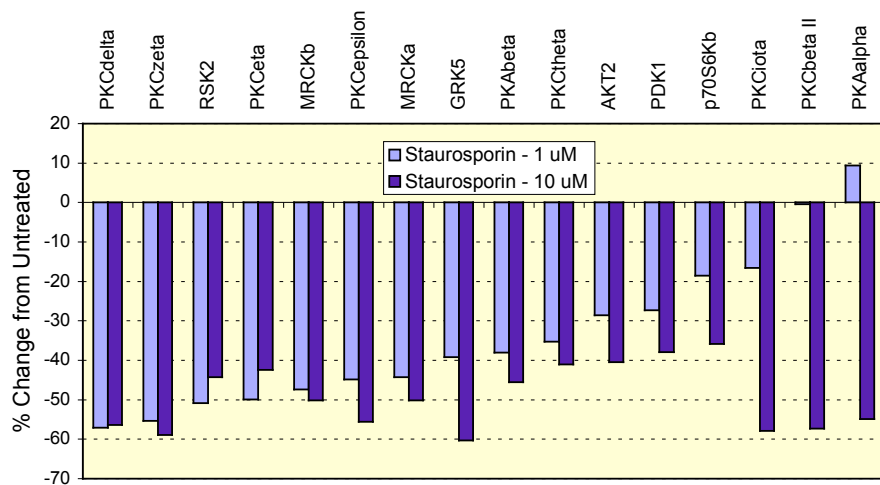
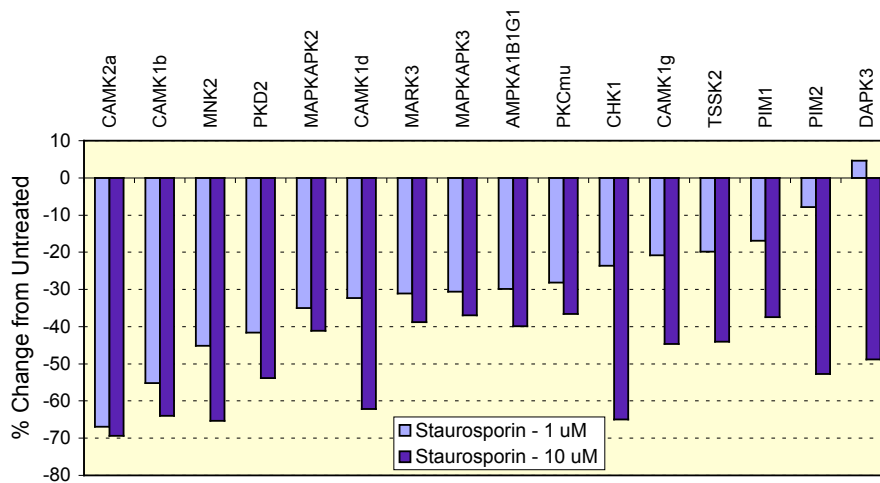


Figure 4A. Kinex™ Protein Kinase Microarray-200 Inhibitor Screening with Staurosporine.

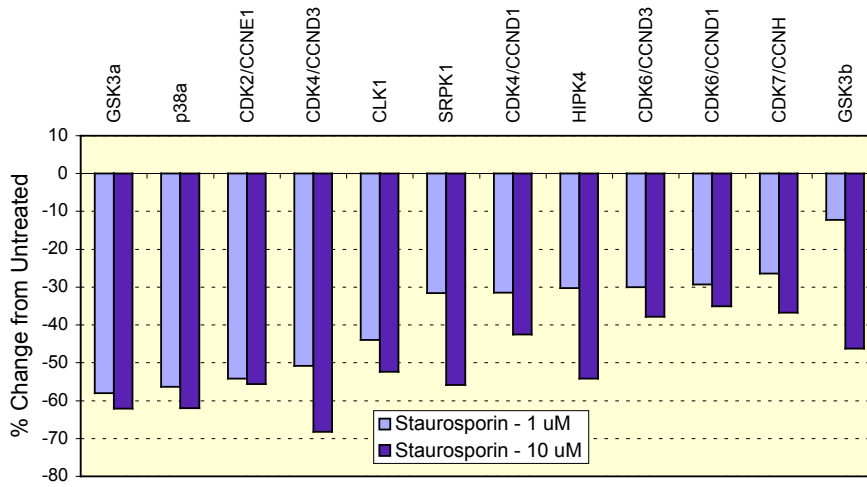


AGC Family Protein Kinases

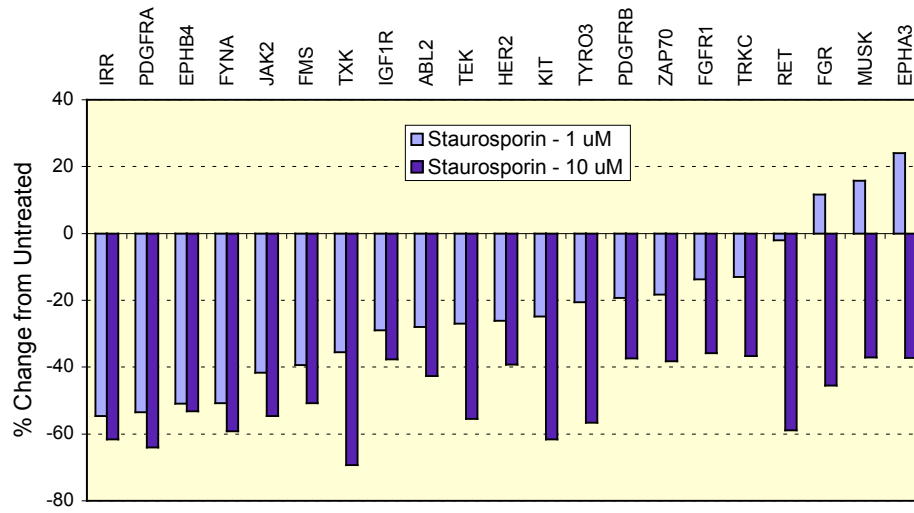


CAMK Family Protein Kinases

Figure 4B. Kinex™ Protein Kinase Microarray-200 inhibitor screening with Staurosporine.



CMGC Family Protein Kinases



TK Family Protein Kinases

Figure 4C. Kinex™ Protein Kinase Microarray-200 Inhibitor Screening with Staurosporine.

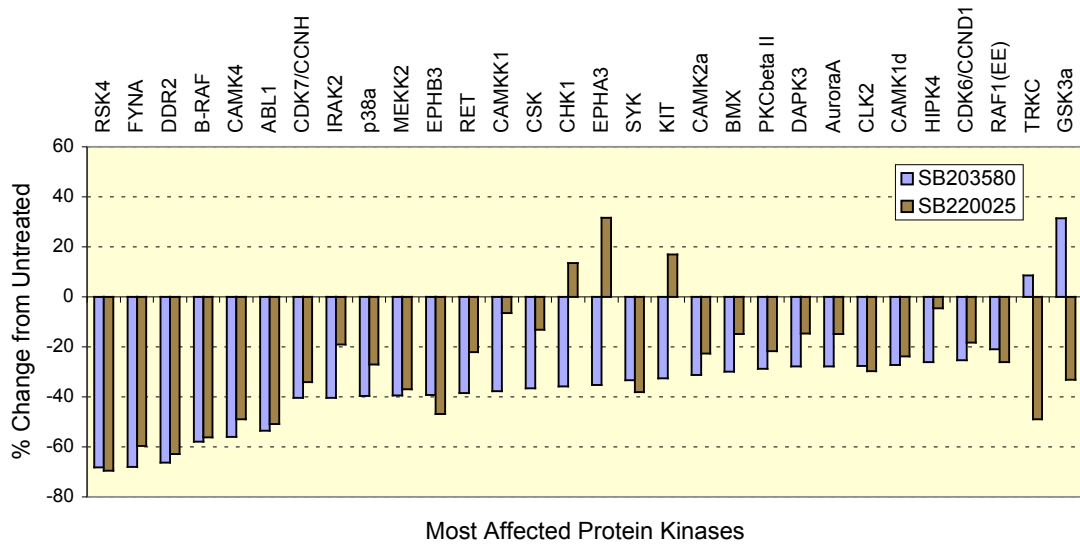


Figure 5. Kinex™ Protein Kinase Microarray-200 inhibitor screening with 5 μ M SB203580 or SB220025.

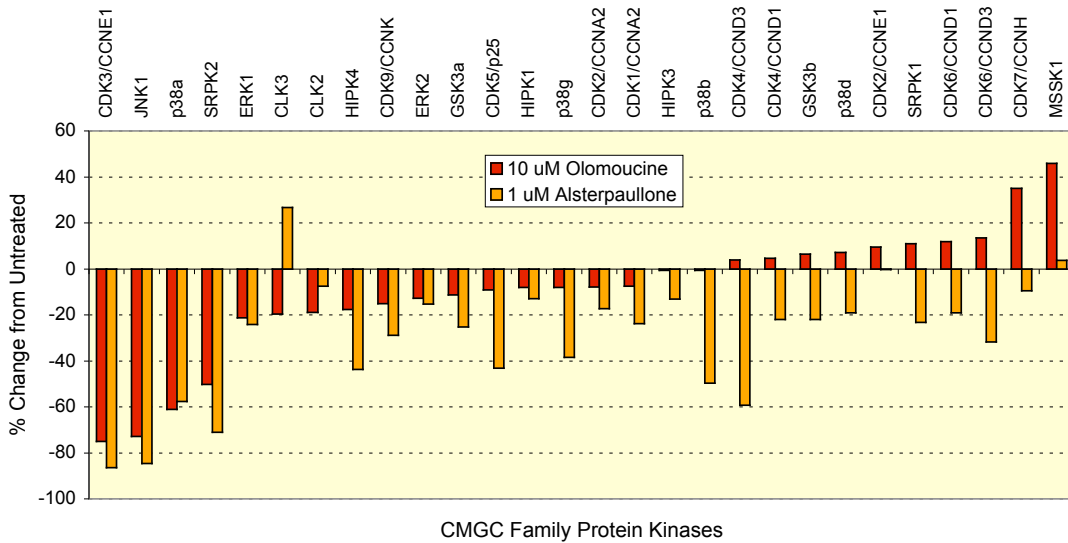


Figure 6. Kinex™ Protein Kinase Microarray-200 inhibitor screening with 10 μ M Olomoucine or 1 μ M Alsterpaullone on CMGC Family protein kinases.

5. KINASE SUBSTRATE PROFILING WITH THE KINEX™ PROTEIN KINASE MICROARRAY-200

The protein kinases on the Kinex™ Protein Kinase Microarray–200 can be used as test substrates for specific protein kinases of interest. Moreover, following their phosphorylation, it is feasible to determine whether the ATP binding ability of the phosphorylated kinases are altered using our ATP analogue probe. In the example provided in Figure 7, we demonstrate the ability of the protein kinase TBK1 to phosphorylate the other protein kinases on the microarray. With this method, the added TBK1 was incubated with one of the grids on the kinase microarray in the presence of ATP. To visualize the phosphorylation of the kinases on the microarray, it was subsequently probed with ProDiamond Q stain (Invitrogen) (Figure 7). When an adjacent grid on the same microarray was incubated with ATP in the absence of any added TBK1, only weak detection on autophosphorylation was evident (data not shown).

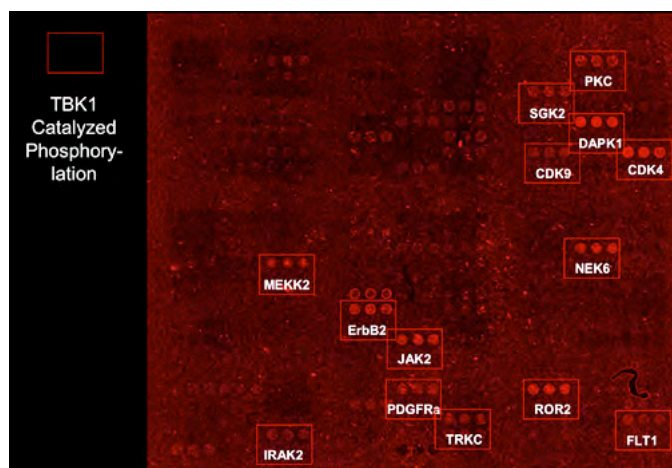


Figure 7. TBK1 phosphorylation of the Kinex™ Protein Kinase Microarray-200 detected with ProQ Diamond stain (Invitrogen).

Our clients can have Kinexus test specific kinases of interest to determine if any of the protein kinases on the Kinex™ Protein Kinase Microarray–200 are direct substrates and ascertain whether this affects the ATP binding ability of the phosphorylated proteins. Clients can supply their own preparations of protein kinases or choose from the list of over 358 different protein kinases in 430 preparations as shown in Table 5.

Table 5. Protein kinases available from Kinexus for substrate profiling on the Kinex™ Protein Kinase Microarray–200. This list may change with respect to availability and pricing.

Protein Kinase Name	Code	U.S. Price	Protein Kinase Name	Code	U.S. Price
Abl1	ABL1	\$200.00	BUBR1(BUB1B)	BU01	\$600.00
Abl1 [E255K]	AB02	\$400.00	CaMK1δ (CAMK1D)	CM1D	\$200.00
Abl1 [G250E]	AB03	\$400.00	CAMK1γ	CM1G	\$200.00
Abl1 [H369P]	AB04	\$600.00	CAMK2α (CAMK2B)	CM2A	\$200.00
Abl1 [T315I]	AB05	\$400.00	CaMK2β (CAMK2B)	CM2B	\$200.00
Abl1 [Y253F]	AB06	\$400.00	CaMK2δ (CAMK2D)	CM2D	\$200.00
Abl1 [M351T]	AB07	\$600.00	CaMK2γ (CAMK2G)	CM2G	\$200.00
Abl1 [Q252H]	AB08	\$600.00	CAMK3γ	CA09	\$200.00
Abl2 (Arg)	ABL2	\$200.00	CAMK4	CMK4	\$200.00
ACK	ACK1	\$200.00	CAMK4 (CaMKIV)	CA11	\$400.00
ACVR1 (ALK2)	AC02	\$400.00	CAMKK1 (CAMKK-alpha)	CKK1	\$200.00
ACVRL1	AC03	\$400.00	CAMKK2	CKK2	\$200.00
ADRBK1 (GRK2)	AD01	\$200.00	CAMKK2 (CaMKK-beta)	CA14	\$400.00
ADRBK2 (GRK3)	AD02	\$400.00	CDC42 BPA (MRCKA)	CD01	\$400.00
Akt1/PKBα	AKT1	\$200.00	CDC42 BPB (MRCKB)	CD02	\$400.00
Akt1/PKBα [dPH, S473D]	AK02	\$600.00	CDC7/ASK	CD03	\$600.00
Akt1/PKBα [dPH]	AK03	\$600.00	CDK1/Cyclin B1	C1B1	\$200.00
Akt2/PKBβ	AKT2	\$200.00	CDK1/CyclinA2	C1A2	\$200.00
Akt2/PKBβ [dPH, S474D]	AK05	\$600.00	CDK2/Cyclin A1	C2A1	\$200.00
Akt3/PKBγ	AKT3	\$200.00	CDK2/Cyclin E1	C2E1	\$200.00
Akt3/PKBγ [S472D]	AK07	\$600.00	CDK2/CyclinA2	C2A2	\$200.00
ALK1	ALK1	\$200.00	CDK3/Cyclin E1	C3E1	\$200.00
ALK4 (ACVR1B)	AL02	\$200.00	CDK4//Cyclin D3	C4D3	\$200.00
AMPKα1/β1/γ1 (PRKAA1/B1/G1)	AM11	\$200.00	CDK4/Cyclin D1	C4D1	\$200.00
AMPKα1/β1/γ2 (PRKAA1/B1/G2)	AM12	\$200.00	CDK5	CD12	\$600.00
AMPKα1/β1/γ3 (PRKAA1/B1/G3)	AM13	\$200.00	CDK5/p25	C5P2	\$200.00
AMPKα1/β2/γ1 (PRKAA1/B2/G1)	AM21	\$200.00	CDK5/p35	C5P3	\$200.00
AMPKα2/β1/γ1 (PRKAA2/B1/G1)	AP11	\$200.00	CDK6/Cyclin D3	C6D3	\$200.00
Ark5	AR01	\$600.00	CDK6/Cyclin D1	C6D1	\$200.00
Ask1 (MAP3K5)	ASK1	\$200.00	CDK7/Cyclin H1/MAT1	C7H1	\$200.00
Aurora A (AurA, AURKA)	AUR1	\$200.00	CDK8/Cyclin C	CD18	\$400.00
Aurora B (AurB, AURKB, INCENP)	AUR2	\$200.00	CDK9/Cyclin K	C9CK	\$200.00
Aurora C (AurC, AURKC)	AUR3	\$200.00	CDK9/Cyclin T1	CD20	\$400.00
Axl	AXL1	\$200.00	CGK2 (PRKG2)	CG01	\$600.00
BARK1 (ADRBK1)	GRK1	\$200.00	CHK1 (CHEK1)	CHK1	\$200.00
BARK2 (ADRBK2)	BA02	\$600.00	CHK2 (CHEK2)	CHK2	\$200.00
Bik	BLK1	\$200.00	CK1α1 (CSNK1A1)	CK01	\$400.00
BMPR1A (ALK3)	BM01	\$600.00	CK1δ (CSNK1D)	CK02	\$400.00
BMPR1B (ALK6)	BM02	\$600.00	CK1δ (CSNK1D) [1-294]	CK03	\$600.00
Bmx	BMX1	\$200.00	CK1ε (CSNK1E)	CK04	\$400.00
B-Raf	RAF2	\$200.00	CK1γ1 (CSNK1G1)	CK05	\$400.00
B-Raf [d1-415]	BR02	\$600.00	CK1γ2 (CSNK1G2)	CK06	\$400.00
B-Raf [V599E]	RAF4	\$200.00	CK1γ3 (CSNK1G3)	CK07	\$400.00
Brk (PTK6)	BR04	\$200.00	CK1γ3 (CSNK1G3)	CK08	\$400.00
BrSK1 (SAD1)	BR05	\$400.00	CK2α1 (CSNK2A1)	CK21	\$200.00
BrSK2	BR06	\$600.00	CK2α2 (CSNK2A2)	CK22	\$200.00
Btk	BT01	\$200.00	CLK1	CLK1	\$200.00
Btk [E41K]	BT01	\$600.00	CLK2	CLK2	\$200.00
Btk [R28H]	BT02	\$600.00	CLK3	CLK3	\$200.00

Table 5. Continued.

Protein Kinase Name	Code	U.S. Price	Protein Kinase Name	Code	U.S. Price
CLK4	CL04	\$400.00	FGFR1 (FLT2) [V561M]	FGRM	\$200.00
COT (MAP3K8)	COT1	\$200.00	FGFR2	FGR2	\$200.00
CRIK	CR01	\$600.00	FGFR2 [N549H]	FG04	\$600.00
Csk	CSK1	\$200.00	FGFR3	FGR3	\$200.00
C-TAK1	CT01	\$600.00	FGFR3 [K650E]	FG06	\$400.00
CTK	CT02	\$600.00	FGFR3 [K650M]	FG07	\$600.00
DAPK1	DAP1	\$200.00	FGFR4	FGR4	\$200.00
DAPK2	DAP2	\$200.00	Fgr	FGR1	\$200.00
DAPK3 (ZIPK)	DAP3	\$200.00	Flt1 (VEGFR1)	FLT1	\$200.00
DCAMKL1	DC01	\$600.00	Flt3	FLT3	\$200.00
DCAMKL2 (DCK2)	DCA2	\$200.00	Flt3 [D835Y]	FL03	\$400.00
DDR1	DD01	\$600.00	Flt4 (VEGFR3)	FL04	\$200.00
DDR2	DDR2	\$200.00	Fms (CSF1R)	FMS1	\$200.00
DLK (MAP3K12)	DL01	\$600.00	FRAP1 (mTOR)	FR01	\$600.00
DMPK1 (DMPK)	DMPK	\$200.00	FRK (PTK5)	FRK1	\$200.00
DRAK1 (STK17A)	DR01	\$600.00	FynA	FYN1	\$200.00
DYRK1A	DY1A	\$200.00	GCK	GCK1	\$200.00
DYRK1B	DY02	\$400.00	GRK4	GR01	\$400.00
DYRK2	DY03	\$600.00	GRK5 (GPRK5)	GRK5	\$200.00
DYRK3	DYR3	\$200.00	GRK6	GRK6	\$200.00
DYRK4	DY05	\$400.00	GRK7	GRK7	\$200.00
eEF2K	EF2K	\$200.00	GSK3 α	GS3A	\$200.00
EGFR (ErbB1)	EG01	\$400.00	GSK3 β	GS3B	\$200.00
EGFR (ErbB1) [L858R]	EG02	\$400.00	Haspin (GSG2)	HA01	\$200.00
EGFR (ErbB1) [L861Q]	EG03	\$400.00	Hck	HC01	\$200.00
EGFR (ErbB1) [T790M, L858R]	EG04	\$400.00	Hgk (MAP4K4)	HG01	\$400.00
EGFR (ErbB1) [T790M]	EG05	\$400.00	HIPK1 (Myak)	HIP1	\$200.00
EIF2AK3 (PERK)	EI06	\$400.00	HIPK2	HI02	\$200.00
EphA1	EPA1	\$200.00	HIPK3	HIP3	\$200.00
EphA2	EPA2	\$200.00	HIPK4	HIP4	\$200.00
EphA3	EPA3	\$200.00	IGF1R	IGF1	\$200.00
EphA4	EPA4	\$200.00	IGF1R [d1-958]	IG02	\$600.00
EphA5	EP05	\$400.00	IKK α (CHUK)	IK01	\$200.00
EphA6	EPA6	\$200.00	IKK β (IKBKB)	IK02	\$200.00
EphA7	EP07	\$600.00	IKK ϵ (IKBKE)	IK03	\$400.00
EphA8	EP08	\$600.00	INSRR (IRR)	ISRR	\$200.00
EphA9	EP09	\$400.00	Insulin Rec. (INSR)	INSR	\$200.00
EphB1	EPB1	\$200.00	IRAK1	IR01	\$600.00
EphB2	EPB2	\$200.00	IRAK2	IRA2	\$200.00
EphB3	EPB3	\$200.00	IRAK4	IRA4	\$200.00
EphB4	EPB4	\$200.00	Itk	ITK1	\$200.00
ErbB2 (HER2, Neu)	ERB2	\$200.00	JAK1	JA01	\$600.00
ErbB4 (HER4)	ERB4	\$200.00	JAK2	JA02	\$200.00
Erk1 (MAPK3)	ERK1	\$200.00	JAK2 [JH1, JH2, V617F]	JA03	\$600.00
Erk2 (MAPK1)	ERK2	\$200.00	JAK2 [JH1, JH2]	JA04	\$400.00
Erk5 (MAPK7)	ER05	\$200.00	JAK3	JAK3	\$200.00
FAK (PTK2)	FAK1	\$200.00	JNK1 (MAPK8) (mouse)	JNK1	\$200.00
Fer	FER1	\$200.00	JNK2 (MAPK9)	JNK2	\$200.00
Fes (Fps)	FES1	\$200.00	JNK3 (MAPK10)	JNK3	\$200.00
FGFR1 (FLT2)	FGR1	\$200.00	KDR (VEGFR2)	KDR1	\$200.00

Table 5. Continued.

Protein Kinase Name	Code	U.S. Price	Protein Kinase Name	Code	U.S. Price
KHS1(MAP4K5)	KHS1	\$200.00	MKK7 β 1 (MKK7 β 1, MAP2K7B1)	MK06	\$600.00
Kit	KIT1	\$200.00	MLCK (MLCK2, MYLK)	ML01	\$200.00
Kit [D816H]	KI02	\$600.00	MLK1 (MAP3K9)	MLK3	\$200.00
Kit [D816V]	KI03	\$600.00	MLK2 (MAP3K10)	ML03	\$200.00
Kit [T670I]	KI04	\$400.00	MLK3 (MAP3K11)	ML04	\$200.00
Kit [V560G]	KI05	\$200.00	MNK1 (MKNK1)	MNK1	\$200.00
Kit [V654A]	KITM	\$200.00	MNK2 (MKNK2)	MNK2	\$200.00
Lck	LCK1	\$200.00	MOS	MO01	\$600.00
LIMK1	LIM1	\$200.00	MRCKa (CDC42BPA)	MRCA	\$200.00
LIMK2	LI02	\$400.00	MRCKb (CDC42BPB)	MRCB	\$200.00
LKB1 (MO25 α , STRADa, STK11)	LKB1	\$200.00	MSK1 (RPS6KA5)	MSK1	\$200.00
LOK (STK10)	LO01	\$600.00	MSK2 (RPS6KA4)	MS02	\$600.00
LRRK2	LRR2	\$200.00	MSSK1 (STK23)	MSS1	\$200.00
LRRK2 [G2019S]	LR02	\$400.00	MST1 (STK4)	MST1	\$200.00
LTK (TYK1)	LT01	\$400.00	MST2 (STK3)	MST2	\$200.00
Lyn A	LYNA	\$200.00	MST3 (STK24)	MST3	\$200.00
Lyn B	LYNB	\$200.00	MST4	MST4	\$200.00
MKK5 (MEK5, MAP2K5)	MK01	\$600.00	MUSK	MUSK	\$200.00
MAP3K14 (NIK)	MA01	\$600.00	MYLK2 (skMLCK)	MY01	\$400.00
MEKK3 (MAP3K3)	ME01	\$200.00	MYO3b	MY03	\$200.00
MAP3K4	MA02	\$600.00	MYT1 (PKMYT1)	MYT1	\$200.00
MAP3K7-MAP3K7IP1 (TAK1-TAB1)	MA03	\$400.00	NDR1 (STK38)	NDR1	\$200.00
GCK (MAP4K2)	GC01	\$400.00	NEK1	NE01	\$200.00
MAP4K4 (HGK)	MA04	\$600.00	NEK11 (FLJ23495)	NK11	\$200.00
MAPKAPK2	MKA2	\$200.00	NEK2	NK02	\$200.00
MAPKAPK3	MKA3	\$200.00	NEK3	NK03	\$200.00
MAPKAPK5 (PRAK)	MKA5	\$200.00	NEK4	NE05	\$400.00
MARK1 (MARK)	MAR1	\$200.00	NEK6	NK06	\$200.00
MARK2	MAR2	\$200.00	NEK7	NK07	\$200.00
MARK3	MAR3	\$200.00	NEK9	NK09	\$200.00
MARK4	MAR4	\$200.00	NLK	NL01	\$400.00
MATK (HYL)	MA12	\$400.00	NUAK1 (ARK5)	NU01	\$400.00
MEK1 (MKK1, MAP2K1)	MEK1	\$200.00	p38 α (MAPK14)	P38A	\$200.00
MEK1 (MKK1, MAP2K1) [S218E, S222E]	MEKA	\$200.00	p38 α (MAPK14) [T106M]	MA14	\$400.00
MEK2 (MKK2,MAP2K2)	MEK2	\$200.00	p38 β (MAPK11)	P38B	\$200.00
MEKK2 (MAP3K2)	MKK2	\$200.00	p38 δ (MAPK13)	P38D	\$200.00
MEKK3 (MAP3K2)	MKK3	\$200.00	p38 γ (MAPK12)	P38G	\$200.00
MELK	ME06	\$400.00	p70S6K (RPS6KB1)	P70A	\$200.00
MERTK (Mer)	MER1	\$200.00	p70S6K (RPS6KB1) [T412E]	RS02	\$400.00
Met	MET1	\$200.00	p70S6K β (RPS6KB2)	P70B	\$200.00
Met [M1250T]	ME09	\$200.00	PAK1/CDC42	PAK1	\$200.00
Met [Y1235D]	ME10	\$400.00	PAK2 (PAK65)	PAK2	\$200.00
MGC42105	MG01	\$200.00	PAK3	PAK3	\$200.00
MINK1 (MINK, ZC3)	ZC03	\$200.00	PAK4	PAK4	\$200.00
MKK3 (MEK3, MAP2K3)	MK01	\$200.00	PAK5 (KIAA1264, PAK7)	PAK5	\$200.00
MKK4 (MEK4, MAP2K4)	MK02	\$400.00	PAK6	PAK6	\$200.00
MKK6 (MEK6, MAP2K6)	MK03	\$200.00	PAR-1B α /MARK2	MAR2	\$200.00
MKK6 (MEK6, MAP2K6) [S599D, T603D]	MK04	\$600.00	PASK	PASK	\$200.00
MKK7 α 1 (MEK7 α 1, MAP2K7A1)	MK05	\$400.00	PBK (TOPK)	PBK1	\$200.00

Table 5. Continued.

Protein Kinase Name	Code	U.S. Price	Protein Kinase Name	Code	U.S. Price
PCTAIRE1 (PCK1)	PC01	\$400.00	Raf1	RAF1	\$200.00
PDGFR α	PDGA	\$200.00	Raf1 (truncated)	RA02	\$600.00
PDGFR α [550-end, D842V]	PD02	\$200.00	Raf1 [Y340D, Y341D]	RA03	\$200.00
PDGFR α [550-end, V561D]	PD03	\$400.00	Ret	RET1	\$200.00
PDGFR α [D842V]	PD04	\$200.00	Ret [V804L]	RE02	\$400.00
PDGFR α [T674I]	PD05	\$600.00	Ret [V804M]	RE03	\$400.00
PDGFR α [V561D]	PD06	\$400.00	Ret [Y791F]	RE04	\$600.00
PDGFR β	PDGB	\$200.00	RIPK2	RIP2	\$200.00
PDHK2 (PDK2)	PD08	\$600.00	RIPK5	RIP5	\$200.00
PDHK3 (PDK3)	PD09	\$200.00	ROCK1 (ROK β)	ROKB	\$200.00
PDHK4 (PDK4)	PD10	\$600.00	ROCK2 (ROK α)	ROKA	\$200.00
PDK1	PDK1	\$200.00	RON (MST1R)	RON1	\$200.00
PEK (EIF2AK3)	PEK1	\$200.00	ROR1	RO04	\$600.00
PhK γ 1 (PHKG1)	PH01	\$400.00	ROR2	RO05	\$400.00
PhK γ 2 (PHKG2)	PHK2	\$200.00	Ros	RO06	\$400.00
Pim1	PIM1	\$200.00	Rse	RO07	\$200.00
Pim2	PIM2	\$200.00	RSK1 (RPS6KA1)	RSK1	\$200.00
Pim3	PI03	\$600.00	RSK2 (PRS6KA3)	RSK2	\$200.00
PKA α (PRKACA)	PKAA	\$200.00	RSK3 (RPS6KA2)	RSK3	\$200.00
PKA β (PRKACB)	PKAB	\$200.00	RSK4 (RPS6KA6)	RSK4	\$200.00
PKA γ (PRKACG)	PKAG	\$200.00	SGK1	SGK1	\$200.00
PKC α (PRKCA)	PKCA	\$200.00	SGK1 [d1-59, S422D]	SG02	\$200.00
PKC β 1 (PRKCB1)	PKC1	\$200.00	SGK2	SGK2	\$200.00
PKC β 2 (PRKCB2)	PKC2	\$200.00	SGK3 (SGKL)	SGK3	\$200.00
PKC δ (PRKCD)	PKCD	\$200.00	SGT220	SG05	\$200.00
PKC ϵ (PRKCE)	PKCE	\$200.00	SGT222-25UG	SG06	\$200.00
PKC γ (PRKCG)	PKCG	\$200.00	SIK	SIK1	\$200.00
PKC η (PRKCH)	PKCH	\$200.00	skMLCK (MYLK2)	SKMK	\$200.00
PKC ι (PRKCI)	PKCI	\$200.00	SLK (STK2)	SLK1	\$200.00
PKC λ (PRKCL)	PKCL	\$200.00	smMLCK (MYLK)	SMMK	\$200.00
PKC α (PRKCQ)	PKCQ	\$200.00	SNF1LK2 (QIK)	SN01	\$200.00
PKC ζ (PRKCZ)	PKCZ	\$200.00	SOK	SO01	\$200.00
PKD1 (PRKD1, PKC μ)	PKD1	\$200.00	Src	SRC1	\$200.00
PKD2 (PRKD2)	PKD2	\$200.00	Src [T341M]	SR02	\$600.00
PKD3 (PRKD3, PRKCN)	PKD3	\$200.00	SRMS (Srm)	SR03	\$600.00
PKG1 α (PRKG1A)	PKG1	\$200.00	SRPK1	SRP1	\$200.00
PKG1 β (PRKG1B)	PK20	\$200.00	SRPK2	SRP2	\$200.00
PKG2 (PRKG2)	PK21	\$600.00	STK16 (PKL12)	ST01	\$400.00
PKN1 (PRK1)	PKN1	\$200.00	STK25 (YSK1)	ST02	\$400.00
PKN2 (PRK2)	PKN2	\$200.00	STK33	ST33	\$200.00
PKR (EIF2AK2)	PKR1	\$200.00	Syk	SY01	\$600.00
PLK1	PLK1	\$200.00	TAK1-TAB1	TAK1	\$200.00
PLK2	PLK2	\$200.00	TAO2	TA01	\$400.00
PLK3	PL03	\$400.00	TAO3	TA02	\$200.00
PLK4	PLK4	\$200.00	TAOK1	TA01	\$200.00
PRKX	PR01	\$600.00	TAOK2 (TAO1)	TA02	\$200.00
PTK5	PT02	\$400.00	TAOK3 (JIK)	TA03	\$200.00
Pyk2 (PTK2B, FAK2)	PYK2	\$200.00	TBK1	TBK1	\$200.00
Raf1 [Y340E, Y341E]	RAFM	\$200.00	TEC	TEC1	\$200.00

Table 5. Continued.

Protein Kinase Name	Code	U.S. Price			
TESK1	TES1	\$200.00			
TGFβR1 (TGFB1, ALK5)	TGF1	\$200.00			
TGFβR2	TGF2	\$200.00			
Tie2 (Tek)	TIE2	\$200.00			
Tie2 (Tek) [R849W]	TI02	\$200.00			
Tie2 (Tek) [Y1108F]	TI03	\$400.00			
Tie2 (Tek) [Y897S]	TI04	\$400.00			
TLK2	TLK2	\$200.00			
TNK1	TN01	\$600.00			
TNK2 (ACK)	TN02	\$600.00			
TrkA (NTRK1)	TRKA	\$200.00			
TrkB (NTRK2)	TRKB	\$200.00			
TrkC (NTRK3)	TRKC	\$200.00			
TSSK1 (STK22D)	TSS1	\$200.00			
TSSK2 (STK22B)	TSS2	\$200.00			
TTBK1	TT01	\$600.00			
TTK	TTK1	\$200.00			
TXK	TXK1	\$200.00			
TYK2	TYK2	\$200.00			
TYRO3 (RSE)	TYR3	\$200.00			
ULK1	ULK1	\$200.00			
ULK2	ULK2	\$200.00			
VRK1	VR01	\$600.00			
Wee1	WEE1	\$200.00			
WNK1	WN01	\$200.00			
WNK2	WN02	\$600.00			
WNK3	WN03	\$600.00			
WNK4	WN04	\$200.00			
YES1	YES1	\$200.00			
ZAK	ZAK1	\$200.00			
ZAP70	ZA02	\$600.00			
ZIPK	ZI01	\$600.00			
ALK2	ALK2	\$200.00			
AMPKα2/β1/γ1 (PRKAA2/B2/G2)	AP22	\$200.00			
CAMK1α (CAMK1)	CM1A	\$200.00			
CAMK1β (PNCK)	CM1B	\$200.00			
CDK1 (CDC2)/CyclinA1	C1A1	\$200.00			
CDK5/p29	C5P9	\$200.00			

6. ANTIBODY PROFILING WITH THE KINEX™ PROTEIN KINASE MICROARRAY-200

The protein kinases on the Kinex™ Protein Kinase Microarray–200 can be used for testing the specificity of antibodies. Figure 8 demonstrates the specificity of the ERK1 antibody that is used in the Kinex™ 800 Antibody Microarray. This pan-specific, rabbit polyclonal antibody developed against the C-terminus of human ERK1 was incubated with one of the grids on the Kinex™ Protein Kinase Microarray–200 and detected with fluorescent dye-conjugated anti-rabbit secondary antibody.

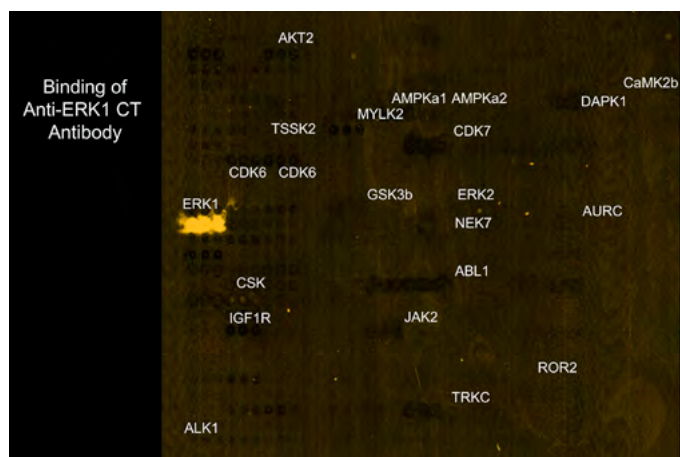


Figure 8. Binding of the ERK1 C-terminus antibody to ERK1 on the Kinex™ Protein Kinase Microarray - 200.

7. DETECTION OF RECOMBINANT PROTEIN BINDING WITH THE KINEX™ PROTEIN KINASE MICROARRAY-200

The Kinex™ Protein Kinase Microarray–200 can be used for testing the ability of proteins and peptides to bind with the protein kinases on the microarray. This can uncover new protein-protein interactions. Figure 9 shows the detection of protein kinases on the Kinex™ Protein Kinase Microarray–200 that bound recombinant glutathione S-transferase (GST) tagged ERK1 through its fluorescent tag.

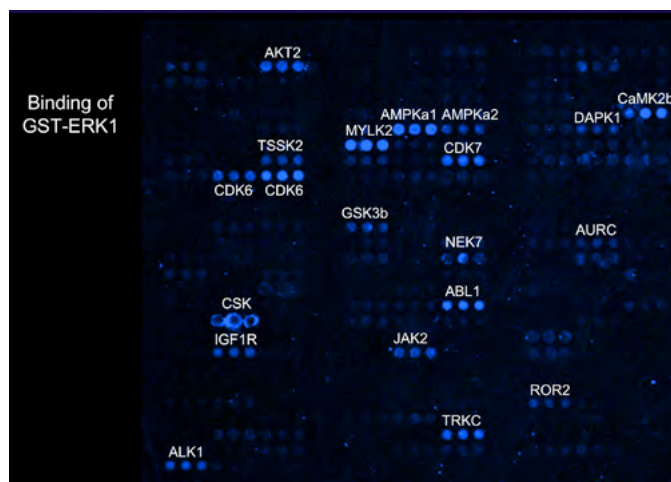


Figure 9. Binding of the GST-ERK1 to protein kinases on the Kinex™ Protein Kinase Microarray-200.

A large body of information and instruction is provided 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 many of the results obtained with our Kinex™ Protein Kinase Microarray – 200 analyses with other scientists in our KiNET DataBank and SigNET Knowledgebank. For these rights, we have discounted our standard prices 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.

8. ORDERING INFORMATION

8.1 Kinex™ Protein Kinase Microarray-based Small Molecule Inhibitor Profiling Service

To place an order for our microarray-based kinase inhibitor profiling services, clients will need to send separate aliquots of their compounds to Kinexus with a copy of the completed “Kinex™ Protein Kinase Microarray-based Small Molecule Inhibitor Profiling Service” order forms. Compounds can be submitted in either powder or solution. Compounds can be dissolved in either phosphate-free aqueous buffer or DMSO. The amount of compound powder to be sent to Kinexus should be sufficient for preparing 1 ml of the solution at the final testing concentration for each assay. The concentration of compound stock solution should be 100 times the final testing concentration. Compounds must be shipped via Fedex or other courier service providers at the expense of the clients. Compounds may be transported at room temperature or frozen, and it should be determined by the clients which is suitable.

Clients should complete the Client-Supplied Non-Confidential Sample Description Form (NSDF-C) provided in this client information package. If you do not wish to provide the requested information, then a Client-Supplied Confidential Sample Description Form (CSDF-C) must be completed, and full confidential pricing charges will be applied. Information requested in the order form is needed for proper handling of the compounds and carrying out the analyses. Completion of the forms to the best knowledge of clients is critical. Due to the presence of 3 incubation fields available for performing assays with the client's compounds, clients may decide to either have the assays performed for the same compound at 3 different concentrations or 3 different compounds (including one of these a control) at single concentrations to make best use of the array and to ensure the comparability of the data between assays. Please indicate your preference for the sample placement on each array (Grid A, B and C), and the final concentration(s) of the compound to be tested in the analyses in the order forms. You should reserve one of these grids for use as the control, which is incubated with the ATP analogue probe in the absence of any other compounds if you plan to use only one kinase microarray chip.

8.2 Kinex™ Protein Kinase Microarray-based Kinase Substrate Profiling Service

To place an order for the Kinex™ Protein Kinase Microarray-based Kinase Substrate Profiling Service, the clients can choose one or more of the protein kinases available in Table 5. Alternatively, the clients may send an aliquot of an active preparation of their protein kinase of interest to Kinexus. In this event, clients should complete the Client-Supplied Non-Confidential Sample Description Form (NKDF-P) provided in this client information package. If you do not wish to provide the requested information, then a Client-Supplied Confidential Sample Description Form (CSDF-P) 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 client-supplied protein kinases are provided as concentrated as possible, preferably at around 10 mg/ml and in *screw cap* vials. We need approximately 2-5 µg of most protein kinases to create at least 750 µl of final testing solution. As there are large variations in the phosphotransferase activity of protein kinases, and every kinase is unique, Kinexus may be able to perform the Kinex™ Kinase Microarray 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 NSDF-P or CSDF-P forms), parafilmed, and then put into another support structure such as a 50-ml conical centrifuge tube to provide extra protection during shipping. Active preparations of test kinases must be shipped via Fedex or other

courier service providers at the expense of the clients. The kinases must be transported frozen, and with sufficient dry ice for at least 4 days if shipped from outside North America.

Information requested in the order form is needed for proper handling of the test kinases and carrying out the analyses. Completion of the forms to the best knowledge of clients will improve the prospects of success with this type of analysis. Due to the presence of 3 incubation fields available for performing assays with the client's compounds, the clients may decide to either have the assays performed for the same kinase at 3 different concentrations or time points or 3 kinases at single concentrations to make best use of the array and to ensure the comparability of the data between assays. Please indicate your preference for the sample placement on each array (Grid A, B and C), and the final concentration(s) of the kinases to be tested in the analyses in the order forms. You may wish to one of these grids for use as the control for autophosphorylation, which is incubated with the ATP in the absence of any added kinases.

8.3 Kinex™ Protein Kinase Microarray-based Protein Interaction Profiling Service

To place an order for our microarray-based protein interaction screening services, clients should send an aliquot of the antibody, recombinant protein or peptide of interest to Kinexus with a copy of the completed "Kinex™ Protein Kinase Microarray-based Protein Interaction Profiling Service" order forms. Clients may also choose to have Kinexus produce recombinant proteins and peptides with our Custom Protein and Peptide Production Services. Proteins (~100 µg) and peptides sent to Kinexus should be sufficient for preparing at least 750 µl of the solution at the final testing concentration for each assay. The concentration of protein or peptide stock solution should be at least 10 times the final testing concentration. Proteins and peptides must be shipped via Fedex or other courier service providers at the expense of the clients. Proteins and peptides may be transported at room temperature or frozen, and it should be determined by the clients which is suitable.

Clients should complete the Client-Supplied Non-Confidential Sample Description Form (NSDF-AB or NSDF-P) provided in this client information package. If you do not wish to provide the requested information, then a Client-Supplied Confidential Sample Description Form (CSDF-AB or CSDF-P) must be completed, and full confidential pricing charges will be applied. Information requested in the order form is needed for proper handling of the test proteins and peptides and carrying out the analyses. Completion of the forms to the best knowledge of clients will improve the prospects of success with this type of analysis. Due to the presence of 3 incubation fields available for performing assays with the client's proteins and peptides, the clients may decide to have the assays carried out for the same protein or peptide at 3 different concentrations or 3 proteins or peptides at single concentrations. Please indicate your preference for the sample placement on

each array (Grid A, B and C), and the final concentration(s) of the peptide/protein to be tested in the analyses in the order forms.

8.4 Turnaround Time

The turnaround time for these services is estimated to be 2 to 3 weeks from the date of receipt of client supplied compounds or proteins by Kinexus. However, this could vary slightly according to the size of the order and the demand of the service at the time when the order is placed. Results of each microarray ordered will be delivered in a comprehensive report consisting of a scanned array image in either jpeg or tiff format and a comparison report for each compound at each concentration against each kinase on the array. Reports are normally delivered electronically to the email addresses of the contact person specified in the order forms.

9. PRICING INFORMATION

Kinexus offers the Kinex™ Kinase Microarray Services at two different pricing levels depending on the level of confidentiality required. The Service Information Form provides the latest standard pricing levels for our Confidential and Non-Confidential Kinex™ Kinase Microarray Services. If the client provides their own compounds, protein kinases, other proteins and/or peptides, only partial information about these materials need to be disclosed in the CSDF forms. To receive a 40% discount off the regular price, Kinexus must be allowed after a minimum 6 month hold to possibly include the results in its on-line KiNET DataBank and SigNET KnowledgeBank, which will permit third parties to access the data.

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. SHIPPING INFORMATION

The aforementioned procedure has been designed to reduce the use of shipping materials and courier costs, and to ensure that your precious compound, peptide or protein 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. For dry ice containing shipments, we recommend Federal Express for shipments originating in North America, and World Express is the preferred courier choice outside of North America. Ship the compounds, peptides or proteins 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 compound, peptide and protein 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.

11. FURTHER INFORMATION ON FORMS TO BE COMPLETED

All of the forms necessary to use the Kinex™ Protein Kinase Microarray Services are provided in the Appendices section of this Customer Information Package. Fillable MS-Word versions of these forms are directly downloadable from the Kinexus website at http://www.kinexus.ca/ourServices/microarrays/microarrays/protein_microarrays.html and by request by e-mail or by phone. Please contact our Technical Service Representatives by email at info@kinexus.ca or by phone at 604-323-2547 Ext. 1 for all enquiries related to technical/research issues, work orders, service fees or request of fillable order forms.

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

- A. Kinexus Proteomics Services Agreement. Customers are required to complete and sign our standard Kinexus Proteomics Services Agreement before their first order can be processed. Unless otherwise specified, this Agreement is valid for all future orders with a standard term of 15 years.
- B. Service Order Form (KPKM-SOF). The Service Order Form (SOF) allows us to obtain client contact and billing information and establish the cost of the order.
- C. Service Identification Form (KPKM-SIF). The Service Identification Form (SIF) permits us to determine which specific Kinex™ Protein Kinase Microarray Services are requested.

If customers wish to send their own compounds, purified protein kinases, proteins and/or peptides, they must also complete and submit one or more the following forms:

- D. Client-Supplied Non-Confidential Sample Description Forms (NSDF-C, NSDF-AB and NSDF-P). Completion of one of these forms may be necessary for qualification for the Non-Confidential pricing discount: NSDF-C for compounds; NSDF-AB for antibodies, NSDF-P for proteins (including kinases) and peptides.
- E. Client Supplied Confidential Sample Description Forms (CSDF-C, CSDF-AB and CSDF-P). Completion of one of these forms may be necessary if the customer wishes to use the fully Confidential services: CSDF-C for compounds; CSDF-AB for antibodies, CSDF-P for proteins (including kinases) and peptides.
- F. Federal Express Airway Bill. For proteins, peptides and compounds to be delivered by Federal Express. Clients can pick any courier of their choice, but from experience, we recommend Federal Express within North America.
- G. Commercial Invoice. This is required for all customers located outside of Canada that send compounds, kinases, other proteins and/or peptides for analysis.

All orders must have as a minimum: 1 SOF and 1 SIF forms completed. A new Kinexus Proteomics Services Agreement may not be necessary if the client has previously placed an order with Kinexus and submitted a signed Kinexus Services Agreement that is still valid. However, we have recently produced an updated Proteomics Services Agreement that is more generalized than previous versions and it provides additional benefits to clients such as extended confidentiality provisions.

FOR ALL CUSTOMERS

A. Kinexus Proteomics Services Agreement

A Kinexus Proteomics Services 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 Proteomics Services 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 (KPKM-SOF)

Please ensure:

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

C. Service Identification Form (KPKM-SIF)

For each Kinex™ Protein Kinase Microarray analysis, please ensure the following:

- In Section A, please specify the particular service required with this microarray.
- In Section B, the customer must assign a unique Client Identification Name for each microarray service used. The samples to be used should also be identified by completion of the appropriate Client-Supplied Sample Description Forms, either NSDF or CSDF, depending on the level of confidentiality.
- Depending on which of the following services are used, please complete either Section C for the KPKM-based Small Molecule Inhibitor Profiling, Section D for the KPKM-based Kinase Substrate Profiling, or Section E for KPKM-based Protein Interaction Profiling. Only one of Sections C, D or E should be completed per KPKM-SIF form.
- Make sure that the Client ID Names in Box A of the various appropriate sample description forms (i.e. NSDF-C, NSDF-P, NSDF-AB, CSDF-C, CSDF-P, and CSDF-AB) matched the Client ID Names in Box B of the KPKM-SIF 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 COMPOUNDS, KINASES,
ANTIBODIES, RECOMBINANT PROTEINS AND/OR PEPTIDES**

D. Client Supplied Sample Description Forms (NSDF-C, NSDF-AB, NSDF-P, CSDF-C, CSDF-AB, CSDF-P)

For submitted samples, please ensure the following:

- Each compound, peptide, protein 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 (KPKM-SIF) to match the sample of compound, peptides or protein to the appropriate grid on the Kinex™ Protein Kinase

Microarray-200. If multiple samples are to be analyzed, enter each of these ID names into Boxes B and C as appropriate on the KPKM-SIF form.

- The form is certified correct and signed and dated.
- Note that some of the information provided on this form will eventually become available to thousands of other scientists in the future with the non-confidentiality pricing. In the spirit of collegiality, please be as accurate as possible in completing the NSDF-C, NSDF-AB or NSDF-P forms in order not to handicap their research efforts should they desire to follow up on your Kinex™ 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 always critical to send compounds, peptides, antibodies and many proteins in a frozen state. However, if you wish to send your samples 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 you or Kinexus with a duty and GST fee on your package. Since the compound or protein 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, which could hold up your order. 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 travel to a Canada Customs facility to claim the package of samples for client order due to inadequate completion of the commercial invoice, additional charges may apply.

12. FOLLOW UP SERVICES

Kinexus offers several services to cost-effectively follow up the results from our Kinex™ Kinase Microarray Services. In particular, the Kinase Inhibitor Compound Profiling (KICP) Service is a convenient and cost-effective follow up for clients to further test the ability of their compounds to inhibit the enzymatic activities of protein kinases from the Kinex™ Kinase Microarray - 200 that demonstrate reduced binding of our ATP analogue probe. To examine the effects of compounds on selected kinases in animals and cells treated with these compounds, 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. More information about specific phosphorylation sites is also freely available from our PhosphoNET KnowledgeBase. 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.



Form: **KPKM-SOF**

KINEX™ PROTEIN KINASE MICROARRAY

SERVICE ORDER FORM

Subject to terms of the Kinexus Proteomics Services Agreement

KINEXUS ORDER NUMBER

CUSTOMER INFORMATION REPEAT CUSTOMER **OR** NEW CUSTOMER

Dr. Mr. Ms. _____
Name of Authorized Representative or Principal Investigator *Title/Position*

Company Name or Institute *Department*

Street Address

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

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

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

KINEX™ PROTEIN KINASE MICROARRAY PROFILING REPORTS

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

REQUESTED WORK AND PRICING INFORMATION

PRICE PER SAMPLE - Refer to Section G of the KPKM Service Identification Forms:		All prices in U.S. Funds
<i>Standard Screens: KPKM-SMIP, KPKM-KSP and KPKM-PIP</i>		
Number of Kinex™ KPKM screens – 3 samples, Non-confidential	= _____ @ \$749 U.S. per screen	\$ _____
Number of Kinex™ KPKM screens – 3 samples, Confidential	= _____ @ \$1099 U.S. per screen	+ \$ _____
<i>Purified Protein Kinases</i>		
Number of protein kinases	= _____ @ \$200 U.S. each	+ \$ _____
Number of protein kinases	= _____ @ \$400 U.S. each	+ \$ _____
Number of protein kinases	= _____ @ \$600 U.S. each	+ \$ _____
Total number of samples submitted with this order: _____	SUBTOTAL	= \$ _____
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 PROTEOMICS SERVICES AGREEMENT AND AGREES TO BE BOUND BY THE TERMS AND CONDITIONS:

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

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



Form: **KPKM-SIF**

**KINEX™ PROTEIN
KINASE MICROARRAY**

SERVICE IDENTIFICATION FORM

Subject to terms of the Kinexus Proteomics Services Agreement

KINEXUS ORDER NUMBER

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

Service Requested:

Use this KPKM-SIF Form for one of the three possible services with the Kinex™ Protein Kinase Microarray. Please refer to the KPKM Services Customer Information Package for further details about these services. Use additional copies of this form for each KPKM chip if you have more samples than three to be tested. If you need assistance completing this form, contact a technical service representative by calling toll free in North America 1-866-KINEXUS (866-546-3987) or by email at info@kinexus.ca.

<p>A. CUSTOM SERVICE REQUESTED: (choose only one)</p> <p><input type="checkbox"/> KPKM-based Small Molecule Inhibitor Profiling (KPKM-SMIP). Complete Section C</p> <p><input type="checkbox"/> KPKM-based Kinase Substrate Profiling (KPKM-KSP). Complete Section D</p> <p><input type="checkbox"/> KPKM-based Protein Interaction Profiling (KPKM-PIP). Complete Section E</p>	<p>KINEXUS ID NUMBER <i>(Bar Code Identification Number)</i></p> <p>For Kinexus Internal Use Only.</p>	<p>B. KPKM-SIF IDENTIFICATION NAME:</p> <p>Client ID: _____</p> <p><i>Use this ID name of your choice for your internal reference and completion of the KPKM-SOF form and any Sample Description Forms. Each microarray analysis with 4 grids should have a unique ID Name. This is useful when multiple copies of this KICP-SIF forms are to be used in your order.</i></p>
<p>C. KPKM-based Small Molecule Inhibitor Profiling</p> <p><i>Use this section to identify which compounds described in the accompanying NSDF-C or CSDF-C forms should be tested and where they should be placed on the three available grids on the Kinex™ Protein Kinase Microarray. One grid should be used for the untreated kinases, which serves as the control.</i></p> <p>Grid A: Compound Name: _____ Compound Concentration: _____</p> <p>Grid B: Compound Name: _____ Compound Concentration: _____</p> <p>Grid C: Compound Name: _____ Compound Concentration: _____</p>	<p>F. ASSAY OR INCUBATION TIME: (if appropriate)</p> <p><i>If you have a recommended or required incubation time, please provide this here.</i></p> <p>Assay time (minutes): _____</p>	
<p>D. KPKM-based Kinase Substrate Profiling</p> <p><i>Use this section to identify which <u>protein kinases</u> listed in Table 5 of the KPKM Customer Information Package (give name and code) or supplied by the client and described in the accompanying NSDF-P or CSDF-P forms should be tested and where they should be placed on the three available grids on the Kinex™ Protein Kinase Microarray. One grid should be reserved for the ATP only incubation, which serves as the control.</i></p> <p>Grid A: Kinase Name (and code): _____ Kinase Concentration: _____</p> <p>Grid B: Kinase Name (and code): _____ Kinase Concentration: _____</p> <p>Grid C: Kinase Name (and code): _____ Kinase Concentration: _____</p>	<p>G. PRICING: (Check which pricing is applicable)</p> <p>1. KPKM-SMIP</p> <p><input type="checkbox"/> Non-Confidential = \$749 per chip (up to 3 compounds)</p> <p><input type="checkbox"/> Confidential = \$1099 per chip (up to 3 compounds)</p> <p>2. KPKM-KSP</p> <p><input type="checkbox"/> Non-Confidential = \$749 per chip (3 kinases)</p> <p><input type="checkbox"/> Confidential = \$1099 per chip (3 kinases)</p> <p><input type="checkbox"/> Kinexus-supplied protein kinases – see Table 5 for pricing per kinase. Sum up costs for up to 3 selected kinases.</p> <p>3. KPKM-PIP</p> <p><input type="checkbox"/> Non-Confidential = \$749 per chip (3 proteins/peptides)</p> <p><input type="checkbox"/> Confidential = \$1099 per chip (3 proteins/peptides)</p>	
<p>E. KPKM-based Protein Interaction Profiling</p> <p><i>Use this section to identify which proteins or peptides supplied by the client and described in the accompanying NSDF-P, NSDF-AB, CSDF-P and CSDF-AB forms should be tested and where they should be placed on the three available grids on the Kinex™ Protein Kinase Microarray.</i></p> <p>Grid A: Protein or Peptide Name: _____ Protein or Peptide Concentration: _____</p> <p>Grid B: Protein or Peptide Name: _____ Protein or Peptide Concentration: _____</p> <p>Grid C: Protein or Peptide Name: _____ Protein or Peptide Concentration: _____</p>	<p>F. SPECIAL INSTRUCTIONS:</p> <p>_____</p> <p>_____</p> <p>_____</p> <p>_____</p> <p>_____</p> <p>_____</p> <p>_____</p> <p>_____</p> <p>_____</p> <p>_____</p>	

Name of person completing this form

Email Address/Facsimile Number/ Phone Number

Date (y/m/d)



KINEXUS

Form: NSDF-C

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

KINEXUS ORDER NUMBER

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

Non-Confidential Service Requested and Compound Sample Details:

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

Form section 1: A. CLIENT SCREEN ID NAME + KINEXUS SERVICES NAME; B. COMPOUND DETAILS. Includes fields for Client ID, Kinexus Proteomics Services Name, Kinexus ID Number, Compound name, Mass (mg), Formula Weight, Molarity, Concentration, Volume, Supplied form of compound, and toxicity.

Form section 2: A. CLIENT SCREEN ID NAME + KINEXUS SERVICES NAME; B. COMPOUND DETAILS. Includes fields for Client ID, Kinexus Proteomics Services Name, Kinexus ID Number, Compound name, Mass (mg), Formula Weight, Molarity, Concentration, Volume, Supplied form of compound, and toxicity.

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

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



KINEXUS

Form: NSDF-P

FOR PROTEINS AND PEPTIDES

CLIENT-SUPPLIED NON-CONFIDENTIAL SAMPLE DESCRIPTION FORM

Subject to terms of the Kinexus Proteomics Services Agreement

KINEXUS ORDER NUMBER

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

Non-Confidential Service Requested and Protein or Peptide Sample Details:

Clients have the option of using their own purified proteins and peptides for Kinexus' Proteomics Services with Non-Confidential Pricing if they fully describe the name, purity and source of these proteins (including full name, UniProt ID number, the species that the proteins were expressed in if it is recombinant, the vendor's name and catalogue number if it is commercially sourced) or peptides (with full amino acid sequence). Please note that in the event that clients do not wish to disclose the source or nature of the proteins or peptides they are providing, then Confidential Pricing must apply and they must complete a CSDF-P form instead.

Form section 1: A. CLIENT SCREEN ID NAME + KINEXUS SERVICES NAME; B. PROTEIN OR PEPTIDE IDENTIFICATION; C. PROTEIN DESCRIPTION; D. COMMERCIAL SOURCE; E. RECOMBINANT KINASE INFORMATION; F. PEPTIDE INFORMATION; G. SPECIAL INSTRUCTIONS - Handling and assay.

Form section 2: A. CLIENT SCREEN ID NAME + KINEXUS SERVICES NAME; B. PROTEIN OR PEPTIDE IDENTIFICATION; C. PROTEIN DESCRIPTION; D. COMMERCIAL SOURCE; E. RECOMBINANT KINASE INFORMATION; F. PEPTIDE INFORMATION; G. SPECIAL INSTRUCTIONS - Handling and assay.

I hereby certify that all of the information about proteins or peptides that I provided with this order is correct and accurate to the best of my knowledge.

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



KINEXUS

Form: NSDF-AB

FOR ANTIBODIES **NON-CONFIDENTIAL** CLIENT-SUPPLIED SAMPLE DESCRIPTION FORM

Subject to terms of the Kinexus Proteomics Services Agreement

KINEXUS ORDER NUMBER

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

Non-Confidential Service Requested and Antibody Sample Details:

Please refer to the Customer Information Package for the particular Kinexus proteomics service that you are requesting for details on how to prepare and ship your antibodies to Kinexus for testing. For Non-Confidential pricing you must fully describe the nature of the probing antibodies (including immunogen sequence, the animal species in which the antibody was produced as well as manufacturer's name and catalogue number if it is commercially sourced). Please note that in the event that clients do not wish to disclose the source or nature of the antibodies that they are providing, then Confidential Pricing must apply. Clients must still complete Sections A to C for Confidential analyses. Please check the appropriate tick boxes. If you need assistance completing this form, contact a technical service representative by calling toll free in North America 1-866-KINEXUS (866-546-3987) or by email at info@kinexus.ca.

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

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

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

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



KINEXUS

Form: CSDF-C

FOR COMPOUNDS

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

KINEXUS ORDER NUMBER

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

Confidential Service Requested and Compound Sample Details:

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

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

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

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

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

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

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



KINEXUS

Form: CSDF-P

FOR PROTEINS AND PEPTIDES

CLIENT-SUPPLIED CONFIDENTIAL SAMPLE DESCRIPTION FORM

Subject to terms of the Kinexus Proteomics Services Agreement

KINEXUS ORDER NUMBER

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

Confidential Service Requested and Protein or Peptide Sample Details:

Clients can provide their own purified proteins and peptides for Kinexus' Proteomics Services without describing the true name and source of these proteins and peptides with Confidential Pricing. A substantial discount is available if clients fully describe the name, purity and source of the proteins and peptides, but they should complete the NSDF-P form instead.

Form 1: A. CLIENT SCREEN ID NAME + KINEXUS SERVICES NAME; B. PROTEIN OR PEPTIDE IDENTIFICATION; C. SPECIES OF KINASE ORIGIN; D. SPECIAL INSTRUCTIONS - Handling and assay; KINEXUS ID NUMBER

Form 2: A. CLIENT SCREEN ID NAME + KINEXUS SERVICES NAME; B. PROTEIN OR PEPTIDE IDENTIFICATION; C. SPECIES OF KINASE ORIGIN; D. SPECIAL INSTRUCTIONS - Handling and assay; KINEXUS ID NUMBER

Form 3: A. CLIENT SCREEN ID NAME + KINEXUS SERVICES NAME; B. PROTEIN OR PEPTIDE IDENTIFICATION; C. SPECIES OF KINASE ORIGIN; D. SPECIAL INSTRUCTIONS - Handling and assay; KINEXUS ID NUMBER

I hereby certify that all of the information about proteins or peptides that I provided with this order is correct and accurate to the best of my knowledge.

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

COMMERCIAL INVOICE

DATE OF EXPORTATION	EXPORT REFERENCES <i>(not required)</i>
SHIPPER/EXPORTER	CONSIGNEE Kinexus Bioinformatics Corporation Suite 1, 8755 Ash Street Vancouver, B.C. Canada V6P 6T3 Telephone: (604) 323-2547 Ext. 1 or 10 Facsimile: (604) 323-2548 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 Number:	

NO. OF PKGS	TYPE OF PACKAGING	QUANTITY OF SAMPLES	COMPLETE AND ACCURATE COMMODITY DESCRIPTION	UNIT VALUE
	<input type="checkbox"/> FedEx Letter <input type="checkbox"/> FedEx Pak <input type="checkbox"/> Box <input type="checkbox"/> Other	<i>Total number of 1.5 ml Eppendorf tubes:</i>	Non hazardous, compound samples packaged in 1.5 ml tubes for research and development testing purposes. Samples are not for resale and there is no commercial value.	\$1.00 <i>per sample</i>
TOTAL NO. OF PACKAGES		TOTAL WEIGHT OF PACKAGES		TOTAL DECLARED VALUE \$

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

SIGNATURE AND STATUS OF AUTHORIZED PERSON

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

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

COMMERCIAL INVOICE

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

NO. OF PKGS	TYPE OF PACKAGING	QUANTITY OF SAMPLES	COMPLETE AND ACCURATE COMMODITY DESCRIPTION	UNIT VALUE
	<input type="checkbox"/> FedEx Letter <input type="checkbox"/> FedEx Pak <input type="checkbox"/> Box <input type="checkbox"/> Other	<i>Total number of 1.5 ml Eppendorf tubes:</i>	Non-hazardous, compounds for research and development diagnostic purposes. Samples are not for resale and there is no commercial value. Samples are packaged on Dry Ice, Class 9, UN 1845, Group 3 (____ X ____ kgs).	\$1.00 <i>per sample</i>
TOTAL NO. OF PACKAGES		TOTAL WEIGHT OF PACKAGES		TOTAL DECLARED VALUE
				\$

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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

COMMERCIAL INVOICE

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SHIPPER/EXPORTER	CONSIGNEE Kinexus Bioinformatics Corporation Suite 1, 8755 Ash Street Vancouver, B.C. Canada V6P 6T3 Telephone: (604) 323-2547 Ext. 1 or 10 Facsimile: (604) 323-2548 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 Number:	

NO. OF PKGS	TYPE OF PACKAGING	QUANTITY OF SAMPLES	COMPLETE AND ACCURATE COMMODITY DESCRIPTION	UNIT VALUE
	<input type="checkbox"/> FedEx Letter <input type="checkbox"/> FedEx Pak <input type="checkbox"/> Box <input type="checkbox"/> Other	<i>Total number of 1.5 ml Eppendorf tubes:</i>	Non hazardous, non infectious protein samples packaged in 1.5 ml tubes for research and development testing purposes. Samples are not for resale and there is no commercial value.	\$1.00 <i>per sample</i>
TOTAL NO. OF PACKAGES		TOTAL WEIGHT OF PACKAGES		TOTAL DECLARED VALUE \$

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

SIGNATURE AND STATUS OF AUTHORIZED PERSON

Print Name

Authorized Signature

Title

Date (month/day/year)

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

COMMERCIAL INVOICE

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

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

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

SIGNATURE AND STATUS OF AUTHORIZED PERSON

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

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: _____

RECITALS

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

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

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

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

1. DEFINITIONS

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

2. REQUEST FOR AND DELIVERY OF PROTEOMICS SERVICES

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

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

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

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

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

3. PAYMENTS

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

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

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

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

4. INTELLECTUAL PROPERTY RIGHTS

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

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

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

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

4.5 Ownership of New Intellectual Property.

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

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

5. CONFIDENTIALITY

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

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

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

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

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

6. TERM AND TERMINATION

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

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

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

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

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

6.4 Effect of an Event of Default.

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

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

7. DISCLAIMER OF WARRANTIES AND LIMITATION OF LIABILITY

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

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

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

8. INDEMNIFICATION

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

9. MISCELLANEOUS

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

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

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

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

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

If to Kinexus:

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

If to the Customer:

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

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

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

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

9.8 Dispute Resolution.

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

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

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

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

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

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

Printed Name of Institute or Company

Per: _____
Signature of Authorized Representative

Name: _____
Printed Name of Authorized Representative

Title: _____
Printed Title of Authorized Representative

Date signed: _____

KINEXUS BIOINFORMATICS CORPORATION

Per: _____
Signature of Dr. Steven Pelech

Dr. Steven Pelech

President and Chief Scientific Officer

Date signed: _____