Supporting Information

High-Throughput Screening of Sulfated Proteins by Using a Genome-Wide Proteome Microarray and Protein Tyrosine Sulfation System

Bo-Yu Huang[1], Po-Chung Chen[2], Bo-Han Chen[1], Chen-Chu Wang[1], Hsuan-Fu Liu[1], Yi-Zao Chen[1], Chien-Sheng Chen[2]*, and Yuh-Shyong Yang[1]*

[1]Bo-Yu Huang, Chen-Chu Wang, Bo-Han Chen, Hsuan-Fu Liu, Yi-Zao Chen, Prof. Yuh-Shyong Yang

Department of Biological Science and Technology. National Chiao Tung University. 75 Boai Street, Hsinchu 300 (Taiwan)

Fax: (+886)3-5712121 ext. 56926. E-mail: ysyang@mail.nctu.edu.tw

[2]Po-Chung Chen, Prof. Chien-Sheng Chen.

Graduate Institute of Systems Biology and Bioinformatics. National Central University. 300 Jhongda Rd, Jhongli 320 (Taiwan)

Fax: (+886)3-4227151 ext. 36103. E-mail: cchen103@gmail.com

Table S1. Experimentally identified sulfated proteins reported previously.[a]

Human		Mouse and Rat		Chick	
Sulfated proteins	**Reference**	**Sulfated proteins**	**Reference**	**Sulfated proteins**	**Reference**
Alpha-2-antiplasmin	[1]	Aminopeptidase N	[68]	Gastrin/cholecystokinin-like peptide	[111]
Alpha-chorigonadotropin	[2]	Bone Sialoprotein II	[79]	Procollagen type V	[112]
Alpha fetoprotein	[3]	C-C chemokine receptor type 8	[70]	**Sheep**	
Aminopeptidase N	[4]	CD44 antigen	[71]	Proenkephalin	[79]
Amyloid protein	[5]	Cholecystokinin (CCK)	[72]	Prolactin	[113]
Anti-CXCR4	[6]	Chromogranin-B	[73]	**Antilocapra americana**	
Anti-HIV-1 E51	[7]	Coagulation factor VIII	[33]	Fibrinogen β chain	[75]
C3a anaphylatoxin chemotactic receptor (C3aR)	[8][9]	Complement C4-Beta	[74]	**Anas platyrhynchos**	
C5a anaphylatoxin chemotactic receptor (C5aR)	[10]	Fibrinogen β chain	[75]	Fibrinogen β chain	[75]
C-C chemokine receptor type 1	[11]	Fibrinogen γ chain	[76]	**Insect**	
C-C chemokine receptor type 2	[12]	Fibronectin	[77]	Drosulfakinins	[114][115]
C-C chemokine receptor type 3	[13]	Gastrin	[78]	Glutactin	[116]
C-C chemokine receptor type 4	[11]	Leu-Enkephalin	[79]	Vitellogenin-1 (yolk protein-1)	[117]
C-C chemokine receptor type 5	[14][15][16]	Lumican	[48]	Vitellogenin-2 (yolk protein-2)	[118]
C-C chemokine receptor type 6	[17]	IgG2a- γ chain	[80]	Vitellogenin-3 (yolk protein-3)	[118]
C-C chemokine receptor type 7	[17]	IgM- λ chain	[81]	Callisulfakinin	[119]
C-C chemokine receptor type 8	[18]	Milk fat globule-EGF factor 8 (MFG-E8)	[82]	Sulfakinin	[120]
C-C chemokine receptor type 9	[17]	Nidogen-1	[83]	Leukosulfakinin	[121]
C-C chemokine receptor type 10	[17]	Amidating enzyme (PAM)	[84]	**Ciona intestinalis**	
Chemokine XC receptor 1 (XCR1)	[17]	Proenkephalin	[79]	Cionin	[122]
CX3C chemokine receptor 1	[19]	Rnase 9	[82]	**Caenorhabditis elegans**	
C-X-C chemokine receptor type 1	[20]	Secretogranin II	[73]	Collagen IV (ROL-6)	[123]
C-X-C chemokine receptor type 2	[11]	SGNE1	[85]	**Plant**	
C-X-C chemokine receptor type 3	[21]	Thyroglobulin	[86]	Phytosulfokines	[124]
C-X-C chemokine receptor type 4	[22][23]	Thyroid-stimulating hormone receptor	[87]	Phytosulfokines 3	[125]
C-X-C chemokine receptor type 5	[17]	Vitronectin (s-protein)	[67]	Phytosulfokines 4	[126]
C-X-C chemokine receptor type 6	[17]	**Bovin**		RGFs (Root meristem growth factors)	[127]
Cholecystokinin (CCK)	[24][25]	Chromogranin-A	[88]	PSY1 (plant peptide containing sulfated tyrosine 1)	[128]
Choriogonadotropin alpha chain	[26]	Chromogranin-B	[88]	**Hirudo medicinalis**	
Complement C4-Alpha	[27][28][29]	Coagulation factor X	[89]	Hirudin 1	[129]
Coagulation factor V	[30][31]	Corticotropin-lipotropin	[90]	Hirudin 2	[130]
Coagulation factor VIII	[32][33][34]	Fibrinogen β chain	[91]	**Conus**	
Coagulation factor IX	[35]	Fibromodulin	[92]	Alpha-conotoxin-like EpI	[131]
D6	[11]	Gastrin	[78]	Alpha-conotoxin PnIA	[132]
Dermatan sulfateproteoglycan	[36]	Microfibril-associated glycoprotein 1 (MAGP-1)	[50]	**Marine sponge**	
Dermatopontin	[37]	Peptidyl-glycine alpha-amidating monooxygenase	[93]	MAFp3	[133]
Duffy antigen and receptor for chemokines (DARC)	[38]	Prolactin	[94]	**Mreen algae**	
Endoglycan	[39]	Pro-opiomelanocortin (POMC)	[95]	Pherophorin I	[134]
Keratinocyte growth factor (FGF-7)	[40]	Secretogranin I	[62]	**Virus**	
Fibrinogen γ chain	[41]	Secretogranin II	[62]	GP Varicella-Zoster	[135]
Fibromodulin	[3]	**Frog**		Kaposi's Scarcoma-associated herpesvirus G protein-coupled receptor	[136]
Follicle-stimulating hormone receptor (FSHR)	[42]	Cholecystokinin type 2	[78]	Polyomavirus	[137]
Gastrin	[43][44]	Gastrin/cholecystokinin-like peptide	[78]		
Heparin cofactor 2	[45][46]	Phyllokinin	[96]		
Histatin 1	[47]	Preprocaerulein clone PXC202	[97]		
Lumican	[48]	Preprocaerulein type-1	[98]		
Luteinising hormone receptor (LHR)/chorionic gonadotropin receptor (CGR)	[42]	Preprocaerulein type-3	[99]		
M2B3 antigen	[49]	Preprocaerulein type-4	[100]		
Maltase	[4]	Pro-opiomelanocortin (POMC)	[101]		
Microfibril-associated glycoprotein 1 (MAGP-1)	[50]	Secretogranin-2	[102]		
Nidogen-1	[51]	Wnt5a	[103]		
osteopontin (OPN)	[52]	Wnt11	[104]		
Platelet glycoprotein Ib alpha chain	[53][54]	**Pig**			
Podocalyxin-like protein 2	[55]	Aminopeptidase N	[4]		
Procollagen type II	[56]	Chromogranin-A	[104]		
Procollagen type III	[57]	Coagulation factor VIII	[105]		
Proteoglycan	[58]	Fibrinogen β chain	[106]		
P-selectin glycoprotein ligand 1	[59][60][61]	Maltase-glucoamylase	[4]		
Secretogranin I	[62]	Sucrase-isomaltase	[4]		
Secretogranin II	[63]	Vitronectin	[107]		
Sucrase-isomaltase	[4]	**Rabbit**			
Thyroglobulin	[63]	Aminopeptidase N	[108]		
Thyroid-stimulating hormone receptor	[64]	Fibrinogen β chain	[75]		
Type 1 sphingosine 1-phosphate receptor (S1P1R)	[65]	Heparin cofactor 2	[109]		
Unique cartilage matrix-associated protein	[66]	Vitronectin	[110]		
Vitronectin (s-protein)	[67]				

[a] Searches on the UniProt database yielded 492 sulfated proteins that included several duplicates. After removing the repeated proteins, we obtained approximately 157 sulfated proteins.

Table S2. Control proteins on the *E. coli* proteome microarray.

	Control protein	Purpose
Am Bm An Bn Ao Bo	AntiMouse->5X	Positive control for mouse serum exp and normalization
Em Fm Cn Dn	AntiMouse->10X	Positive control for mouse serum exp and normalization
Cm Dm	AntiHuman->1X	Positive control for human serum exp
En Fn	BiotinHRP->5X	Positive control for streptavidin conjugated molecule and determination
Gm Hm	BiotinHRP->10X	Positive control for streptavidin conjugated molecule and determination
Gn Hn	BiotinHRP->50X	Positive control for streptavidin conjugated molecule and determination
Im Jm	GSH->5X	Positive control for yeast exp and determination
In Jn	GSH->10X	Positive control for yeast exp and determination
Kn Ln	GSH->25X	Positive control for yeast exp and determination
Mm Nm	HSAHis->1X	Positive control for AntiHuman antibody and AntHis antibody
Km Lm	H4->1X	Positive control for proteins
Om Pm	ProteinG->5X	Determination of IgG and normalization
Mn Nn	ProteinG->10X	Determination of IgG and normalization
On Pn	ProteinG->25X	Determination of IgG and normalization
Io Jo	BSA->4.375mM	Negative control of sulfation
Eo Fo	PolyEAY->4mM	Positive control of sulfation
Co Do	PSGL-1->0.3mM	Positive control of sulfation
Mp Np	Glycerol	Negative control
Ko Lo	Cy5-AntiMouseIgM->200X	Landmark for GAL file alignment
Op Pp	Cy3-AntiMouseIgG->200X	Landmark for GAL file alignment

Control proteins: Io, Jo on the chip: BSA, negative control for sulfation; Co, Do and Eo, Fo: PSGL-1 and PolyEAY, respectively, positive controls for sulfation. The other proteins listed were not used in this experiment.

Table S3. Sulfated proteins on the *E. coli* proteome chip, listed according to the rank of the fluorescence signal after ProCAT analysis.

1-10	yfjV	274#3	345#5	ycaO	567#1	tdk	416#1	ynfI	speA	hofC
11-20	yggF	MolR	guaC	era	yafX	priS	amyA	yjeI	mazG	uxaB
21-30	yzzO	yebU	yjeT	lacY	phoE	lguL	purF	infB	yqaE	rrsB
31-40	yicP	hfq	uup	ykgE	ykfC	corA	ycfF	hypE	carA	recC
41-50	mraY	ybiT	242#1	pabB	yafS	403#0.1	ybbZ	ilvH	VPB_BP186	pepN
51-60	flgI	yheS	yqjB	ydiZ	yhbM	fliT	mukF	yqaA	ygjN	yceK
61-70	yahB	ykfF	yhdU	yaiP	sbm	ygeT	relE	yehI	ycdr	JW2995
71-80	caiA	mopA	fhuB	guaB	secA	ptsG	140#9	sbcC	yfjW	yqiI
81-90	dinP	rne	ebr	yfcI	yghK	yacC	paaD	imp	yqiG	ftsW
91-100	yadJ	ydfC	ccmE	apaG	treF	yadM	yfhC	ytfK	hyaF	380#5
101-110	344#15	yqhG	sfsA	325#1	yrfB	phpB	fhiA	fecA	ycfN	csgF
111-120	argG	ycjT	120#5	ycjL	ydfB	smg	yeaA	443#3	yzpU	cca
121-130	yadL	657#1.1	codB	fldB	yagK	abc	yadP	alpA	pntA	hemL
131-140	yagD	yadK	yjdA	thrC	yafD	yahG	prpE	fepA	yehT	ygiC
141-150	yggP	mhpE	yaeC	bifF	ycgC	yjfU	yahL	gadB	yfjN	htrA
151-160	yrfA	yaeD	ykgK	yliG	brnQ	fliG	VPD_BP186	asnB	iciA	nfo
161-170	chuR	yaeJ	yafE	yfjX	mhpF	nuoD	yafC	usg1	348#4	ycfD
171-180	304#4	malS	nhaR	yagT	dnaE	ykgJ	yabM	yfbM	yahE	yafQ
181-190	kefC	nrdE	eutJ	panD	flgK	thrA	yajC	nadA	427#7	purL
191-200	ycdY	yaeG	yaiB	280#2	ybdB	yahC	accA	cmtB	31-11C0	yhcP
201-210	nrdG	yadT	fhuD	ychA	clpP	yndN	hepA	yagW	lpxC	yagA
211-220	hypD	gatY	prmA	mhpR	caiB	yagS	recJ	glgX	yagY	yhjH
221-230	dinJ	yafW	yafT	yhgB	nfrB	ptsO	yedP	29-7G0	ampD	uvrB
231-240	htrE	yoaH	7-6A0	ftsZ	crl	speF	ygiF	leuC	477#7	prn
241-250	yaaC	rpsT	yibJ	yagJ	yadB	yadI	carB	aroM	yhaD	add
251-260	lysC	cyaY	putA	tufA	citE	adi	hybG	speE	cynT	yehB
261-270	17-1A0	caiE	glnQ	yqeV	yabC	ylbE	caiF	yadD	yzzN	ykgG
271-280	queA	yahN	fixA	yagZ	dksA	379#5	yabH	metK	hyfR	tesA
281-290	yafM	shI	phnA	lacZ	caiT	hlpA	sucP	ldcC	trkA	poxB
291-300	speC	potA	yhjW	yciW	rpsI	rpoS	hprT	yafY	yabF	phnB
301-310	icc	tdcB	267#7	32-1G0	dgt	mlc	ydiB	hypF	dapB	pdhR
311-320	hemK	ldhA	yaaV	lytB	ykiA	145#4	403#1	mhpT	pheT	napD
321-330	malY	agaY	fabH	yiiL	aceF	ydhL	yjaG	421#7	hemA	yqhD
331-340	cobB	rhsC	cynR	ybfF	yagP	ybdH	surA	yjiQ	yeiC	yaiA
341-350	pqiB	hmpA	yaaH	yagC	yggW	panB	ybeR	arcA	hybD	cutA
351-360	menF	211#9	ydeH	rhsB	41-1C0	dfp	210#3	folA	ypfH	309#4
361-370	talC	lacI	yliH	hyaD	ynhC	ygeA	164#9	ybhH	entF	yciQ
371-380	yceF	bisZ	yeaG	trpG	ybhN	yrdB	fliN	319#10	ybhA	ybaD
381-390	yehO	ytfS	yihE	purB	ftsA	hybF	ykgF	nuoF	purT	sapC
391-400	glyQ	yfjY	menC	408#4	pgpA	ybeL	356#8	cynS	ddlB	mcrA
401-410	uxuA	411#12	yajO	319#14	238#9	yheK	ribD	flhB	mutY	sdaA
411-420	murC	cchA	citB	parE	celC	araC	323#1	ybeW	smb	cbl
421-430	pflA	murD	211#15	mtlD	ispB	yaaD	ppx	leuD	yafJ	yaiI
431-440	murB	agaZ	ycjK	selD	ygiP	envR	ybeY	ybaP	mutT	yhfN
441-450	rpsB	yigR	yacH	tdh	yhfV	ilvB	lasT	yycB	yfjZ	apaH

451-460	440#5.1	29-5D0	cysM	pfs	nrdF	yabO	tauA	yqcC	yaiM	mukE
461-470	yahA	rnhA	vacJ	ykfI	ruvB	ybeN	ykfA	yeiR	yifB	yliJ
471-480	yiiD	20-3F0	yhcI	453#2	ykgM	vsr	hyaB	dnaG	lipA	sucA
481-490	phoP	lueO	holB	gadA	aceE	cysI	ykgD	yidJ	218#5	yieJ
491-500	437#9	rnd	rocE	glpE	ycjU	thrB	aceK	folK	17-5A0	narW
501-510	fimH	ybbB	ybbN	thiD	pdxA	thiC	nrdB	ydhD	yfiC	phrB
511-520	rplT	mhpA	yjaD	araG	ypjA	lyxK	murF	146#1	acpS	phoB
521-530	yejG	ygjD	ilvI	yrbA	yafA	yajQ	molR	asnS	yfbB	yhcP
531-540	ybjN	nadC	yaiE	uxaC	betI	mutH	ysgA	mioC	ybaJ	ftsQ
541-550	ppsA	rpoE	ybbT	leuA	457#1	trx2	yhaJ	sun	ilvA	yihX
551-560	yjeR	fhlA	ydiU	adhC	asnA	pmrD	yjaB	ybiC	grxA	yhaN
561-570	mhpB	yigZ	torD	yefG	cobU	yafO	yqcD	yacF	yjjG	ycaK
571-580	ybbL	yddH	fliH	leuB	feaB	hypA	29-2H0	ybeF	280#3	polB
581-590	yacE	yceA	ybjF	bioA	316#17	yhcO	amn	ycaR	ycfC	yadR
591-600	21-12A0	cheB	betA	yieH	entA	araD	moeB	576#14	yjfR	glnD
601-610	cutA3	pncB	yhbZ	430#9	ydgB	yaeP	20-10E	perR	nhoA	ybiK
611-620	404#7	malZ	228#10	yajP	ycfO	priC	yehK	trpC	lrhA	sdaB
621-630	yjfW	dsdA	cstC	yjfV	414#5	664#6	yidB	ybfE	ugpQ	gmhA
631-640	hycH	caiD	celA	yqhG	dniR	nuoE	rnhB	ygiP	trmA	fabF
641-650	xylB	phoU	yifI	yiaC	gst	yjjX	glpB	yqeG	efp	yphG
651-660	gloB	yciC	entD	yneI	uncC	tyrB	cmk	hybE	yaeH	recO
661-670	thiM	cfa	ybdL	22-4A0	210#5	yahD	479#2	hemN	fms	yidU
671-680	fadR	yjeK	xylR	yaeR	yahK	trpA	araA	bfr	mesJ	fliS
681-690	yhaF	btuR	ybiU	yhbY	hyaE	znuA/yebL	yajD	cheW	cysG	speD
691-700	ycgY	ybiH	arcM	ribA	metF	ydhB	ydaL	fur	baiF	proB
701-710	bglG	ybhK	fixC	hrpB	ybcO	yccG	yhiN	rfbB	gcpE	yhhP
711-720	soxA	trpB	ygjR	ycdC	ycfX	yaiL	suhB	yggD	paaX	yeaK
721-730	hypC	320#1	fucR	ylbC	ygfY	rpiR	artP	wcaC	yjhH	ychB
731-740	grxC	406#7	caiC	rstA	lysA	hlyU	yaeQ	ubiB	tyrA	fliJ
741-750	otsA	moaE	ybaS	ybdU	275#2	yjiL	bioH	ybbS	acrR	259#3
751-760	459#3	fadD	yciH	ybhJ	fucK	yhgG	recR	ygcN	firA	yjeJ
761-770	ycfB	rbfA	ydaH	mobA	yciE	31-11D0	ptkB	yhfY	yedJ	ddlA
771-780	dcd	cysC	nagB	ylaJ	mog	araB	ntrB	xseB	wzb	aroB
781-790	kbl	oat	hisG	ybaC	aldH	320#2	ads	srlD	eutI	yjfI
791-800	nusB	gpsA	phnP	nagC	thrS	228#9	467#1	31-02	yeiN	livF
801-810	gatD	metR	dga/murI	atoD	327#9	ybiI	dnaC	ygdE	yegS	ybgL
811-820	codA	yagE	dhnA	dpaL	yjgU	yecP	380#2	yfbC	ilvN	aspC
821-830	yciO	ascB	yaeS	yrhB	yccW	405#4	yafV	agaS	yfjB	dapD
831-840	334#5.1	yehV	grpE	ybdQ	ygdH	223#10	ygdK	zwf	yaeL	yraO
841-850	edd	mhpC	ydfG	pnp	ybaW	uidA	prlC	yibF	yaiN	entC
851-860	ycbY	pepT	proW	xylA	trxB	yjgJ	hisI	aroE	yffB	galT
861-870	torC	hemH	merA	ygfG	ylbB	div	yjcT	yaeM	ybgI	apt
871-875	citF	rpiA	pfkA	galE	allA					

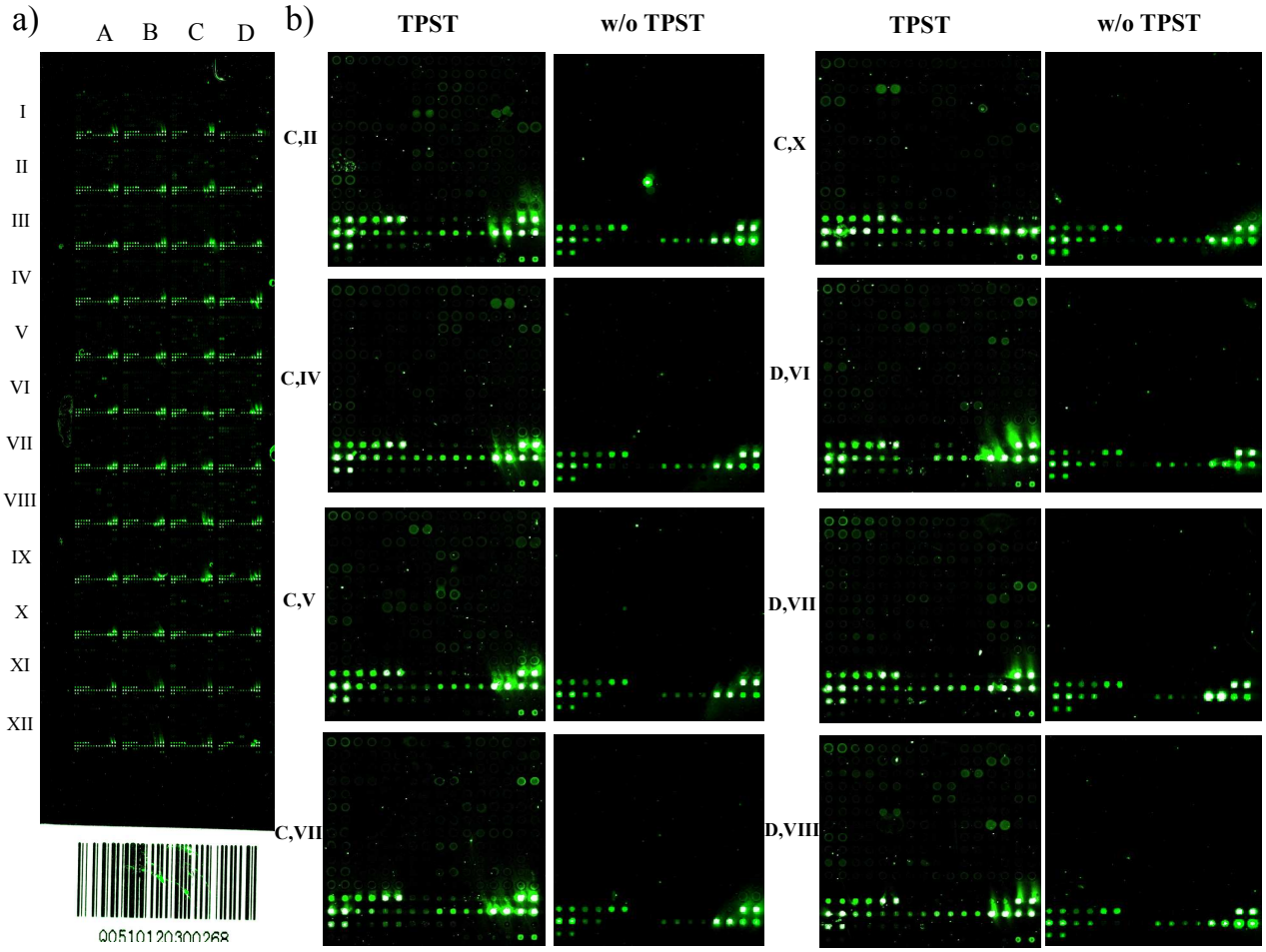

Figure S1. Images of *E. coli* proteome microarrays**.** a) *E. coli* proteome microarray chip containing 48 microarrays. The *E. coli* proteome microarrays were composed of 4256 N-terminal GST-fusion proteins immobilized on nitrocellulose-coated glass slides (FAST slides, Whatman). Each protein was duplicated on the chip.[1] b) Comparisons of 8 protein microarrays (CII, CIV, CV, CVII, CX, DVI, DVII, and DVIII) treated with either the complete PTS coupled-enzyme system (left) or in the absence of the TPST (right).

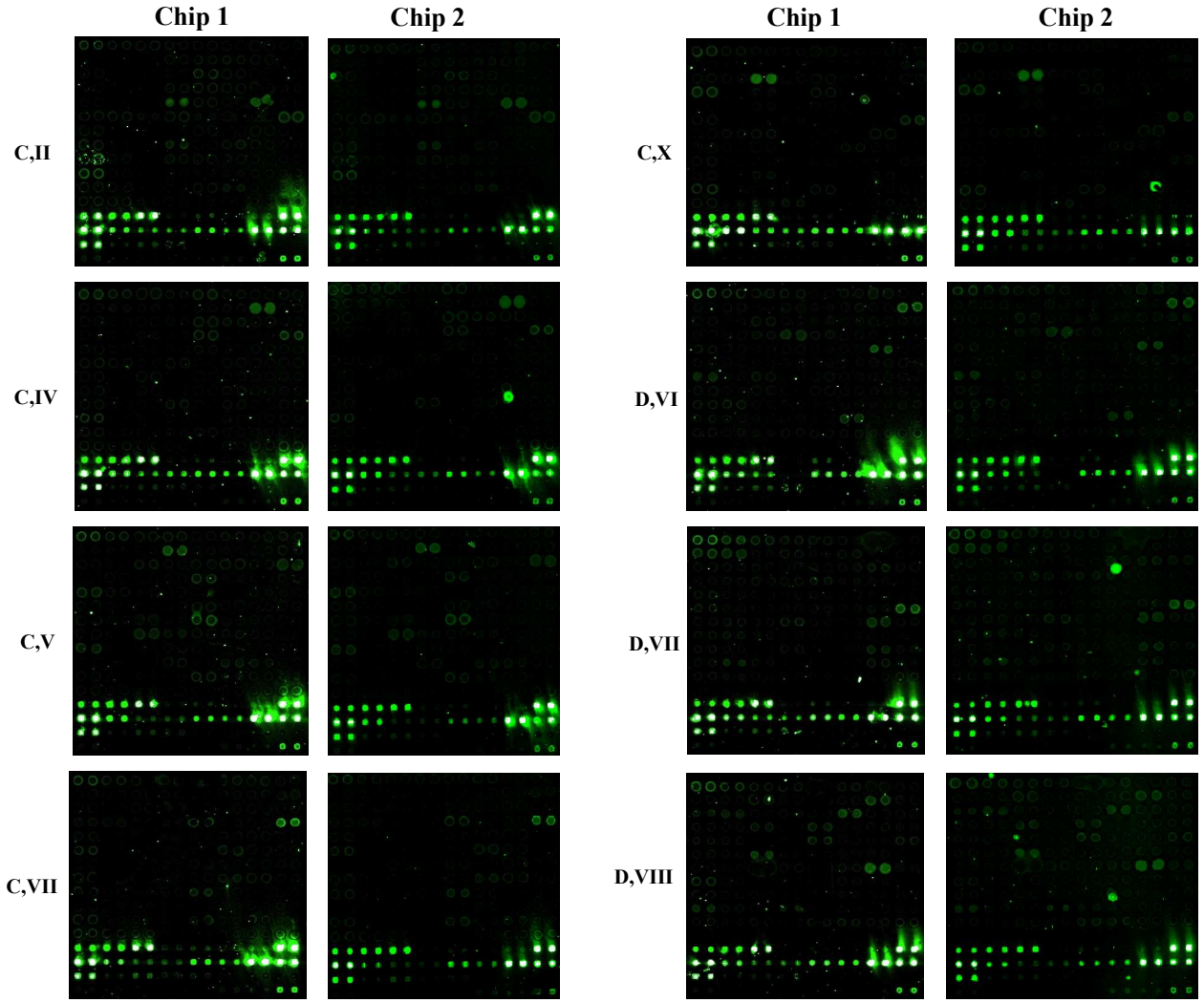

Figure S2. All the proteome chip data presented in this report were triplicated (using separate two sets of the proteome chips for data collection) to confirm their reproducibility. We obtained the same results from all of the two different proteome chips.

Supporting references

[1] G. Hortin, K. F. Fok, P. C. Toren, A. W. Strauss, *J. Biol. Chem.* **1987,** *262*, 3082–3085.

[2] M. Bielinska, *Biochem. Biophys. Res. Co.* **1987,** *148*,1446–1452.

[3] M. C. Liu, S. Yu, J. Sy, C. M. Redman, F. Lipmann, *Proc. Natl. Acad. Sci. USA.* **1985,** *82*, 7160–7164.

[4] E. M. Danielsen, *EMBO J.* **1987,** *6*, 2891–2896.

[5] A. Weidemann, G. König, D. Bunke, P. Fischer, J. M. Salbaum, C. L. Masters, K. Beyreuther, *Cell* **1989,** *57*, 115–126.

[6] C. Xu, J. Sui, H. Tao, Q. Zhu, W. A. Marasco, *J. Immunol.* **2007,** *15*, 2408–2418.

[7] H. Choe, et al., *Cell* **2003,** *114*, 161–170.

[8] C. Seibert, T. P. Sakmar, *Biopolymers* **2008,** *90*, 459–477.

[9] J. Gao, H. Choe, D. Bota, P. L. Wright, C. Gerard, N. P. Gerard, *J. Biol. Chem.* **2003,** *278*, 37902–37908.

[10] M. Farzan, C. E. Schnitzler, N. Vasilieva, D. Leung, J. Kuhn, C. Gerard, N. P. Gerard, H. Choe, *J. Exp. Med.* **2001,** *193*, 1059–1065.

[11] J. Liu, S. Louie, W. Hsu, K. M. Yu, H. B. Nicholas Jr., G. L. Rosenquist, *Am. J. Respir. Cell Mol. Biol.* **2008**, *38*, 738–743.

[12] A. A. Preobrazhensky, S. Dragan, T. Kawano, M. A. Gavrilin, I. Gulina, L. Chakravarty, P. E. Kolattukudy, *J. Immunol.* **2000**, *165*, 5295–5303.

[13] J. Z. Zhu, C. J. Millard, J. P. Ludeman, L. S. Simpson, D. J. Clayton, R. J. Payne, T. S. Widlanski, M. J. Stone, *Biochemistry* **2011,** *50*, 1524–1534.

[14] M. Farzan, T. Mirzabekov, P. Kolchinsky, R. Wyatt, M. Cayabyab, N. P. Gerard, C. Gerard, J. Sodroski, H. Choe, *Cell* **1999**, *96*, 667–676.

[15] L. Duma, D. Häussinger, M. Rogowski, P. Lusso, S. Grzesiek, *J. Mol. Biol.* **2007**, *365*, 1063–1075.

[16] C. Seibert, M. Cadene, A. Sanfiz, B. T. Chait, T. P. Sakmar, *Proc. Natl. Acad. Sci. USA.* **2002,** *99*, 11031–11036.

[17] M. J. Stone, S. Chuang, X. Hou, M. Shoham, J. Z. Zhu, *N Biotechnol* **2009,** *25*, 299–317.

[18] J. Gutiérrez, L. Kremer, A. Zaballos, I. Goya, A. C. Martínez, G.

Márquez, *J. Biol. Chem.* **2004,** *279*, 14726–14733.
[19] A. M. Fong, S. M., Alam, T., Imai, B. Haribabu, D. D. Patel, *J. Biol. Chem.* **2002,** *277*, 19418–19423.
[20] N. J. Skelton, C. Quan, D. Reilly, H. Lowman, *Structure* **1999,** *7*, 157–168.
[21] R. A. Colvin, G. S. Campanella, L. A. Manice, A. D. Luster, *Mol. Cell Biol.* **2006,** *26*, 5838–5849.
[22] M. Farzan, G. J. Babcock, N. Vasileva, P. L. Wright, E. Kiprilov, T. Mirzabekov, H. Choe, *J. Biol. Chem.* **2002,** *277*, 29484–29489.
[23] C. T. Veldkamp, C. Seibert, F. C., Peterson, T. P. Sakmar, B. F. Volkman, *J. Mol. Biol.* **2006,** *359*, 1400–1409.
[24] V. Mutt, J. E. Jorpes, *Eur. J. Biochem.* **1968,** *6*, 156–162.
[25] R. T. Jensen, G. F. Lemp, J. D. Gardner, *J. Biol. Chem.* **1982,** *257*, 5554–5559.
[26] J. P. Ludeman, M. J. Stone, *Br. J. Pharmacol.* **2014,** *171*, 1167–1179.
[27] D. R. Karp, *J. Biol. Chem.* **1983,** *258*, 12745–12748.
[28] G. Hortin, H. Sims, A. W. Strauss, *J. Biol. Chem.* **1986,** *261*, 1786–1793.
[29] G. L. Hortin, T. C. Farries, J. P. Graham, J. P. Atkinson, *Proc. Natl. Acad. Sci. USA.* **1989,** *86*, 1338–1342.
[30] G. L. Hortin, *Blood* **1990,** *76*, 946–952.
[31] D. D. Pittman, K. N. Tomkinson, D. Michnick, U. Selighsohn, R. J. Kaufman, *Biochemistry* **1994,** *33*, 6952–6959.
[32] A. Leyte, H. B. van Schijndel, C. Niehrs, W. B. Huttner, M. Verbeet, K. Mertens, J. A. van Mourik, *J. Biol. Chem.* **1991,** *266*, 740–746.
[33] D. D. Pittman, J. H. Wang, R. J. Kaufman, *Biochemistry* **1992,** *31*, 3315–3325.
[34] D. A. Michnick, D. D. Pittman, R. J. Wise, R. J. Kaufman, *J. Biol. Chem.* **1994,** *269*, 20095–20102.
[35] M. Bond, et al., *Semin. Hematol.* **1988,** *35*, 11–17.
[36] J. R. Couchman, A. Woods, M. Hook, J. E. Christner, *J. Biol. Chem.* **1985,** *260*, 13755–13762.
[37] E. G. Forbes, A. D., Cronshaw, J. R. E. MacBeath, D. J .S. Hlumes, *FEBS Lett.* **1994,** *351*, 433–436.
[38] H. Choe, M. J. Moore, C. M. Owens, P. L. Wright, N. Vasilieva, W. Li, A. P. Singh, R. Shakri, C. E. Chitnis, M. Farzan, *Mol. Microbiol.* **2005,** *55*, 1413–1422.
[39] C. B. Fieger, C. M. Sassetti, S. D. Rosen, *J. Biol. Chem.* **2003,** *278*, 27390–27398.
[40] Y. R. Hsu, E. W. J. Hsu, V. Katta, D. Brankow, J. Tseng, S. Hu, C. F. Morris, W. C. Kenney, H. S. Lu, *Protein Expr. Purif.* **1998,** *12*, 189–200.
[41] D. H. Farrell, E. R. Mulvihill, S. Huang, D. W. Chung, E. W. Davie, *Biochemistry* **1991,** *30*, 9414–9420.
[42] M. Bonomi, M. Busnelli, L. Persani, G. Vassart, S. Costagliola, *Mol. Endocrinol.* **2006,** *20*, 3351–3363.
[43] H. Gregory, P. M. Hardy, D. S. Jones, G. W. Kenner, R. C. Sheppard, *Nature* **1964,** *204*, 931–933.
[44] J. R. Bundgaard, J. Vuust, J. F. Rehfeld, *EMBO J.* **1995,** *14*, 3073–3079.
[45] G. Hortin, D. M. Tollefsen, A. W. Strauss, *J. Biol. Chem.* **1986,** *261*, 15827–15830.
[46] J. W. Mitchell, F. C. Church, *J. Biol. Chem.* **2002,** *277*, 19823–19830.
[47] T. Cabras, C. Fanali, J. A. Monteiro, F. Amado, R. Inzitari, C. Desiderio, E. Scarano, B. Giardina, M. Castagnola, I. Messana, *J. Proteome. Res.* **2007,** *6*, 2472–2480.
[48] P. K. Cornuet, T. C. Blochberger, J. R. Hassell, *Invest. Ophthalmol. Vis. Sci.* **1994,** *35*, 870–877.
[49] M. B. Omary, L. De Grandpre, N. M. Varki, M. F. Kagnoff, *Mol. Immunol.* **1992,** *29*, 9–19.
[50] B. C. Trask, T. Broekelmann, T. M. Ritty, T. M. Trask, C. Tisdale, R. P. Mecham, *Biochemistry* **2001,** *40*, 4372–4380.
[51] A. D. Westmuckett, A. J. Hoffhines, A. Borghei, K. L. Moore, *Gen. Comp. Endocr.* **2008,** *156*, 145–153.
[52] M. D. McKee, S. Zalzal, A. Nanci, *Anat. Rec.* **1996,** *245*, 293–312.
[53] J. F. Dong, C. Q. Li, J. A. Lopez, *Biochemistry* **1994,** *33*, 13946–13953.
[54] P. Marchese, M. Murata, M. Mazzucato, P. Pradella, L. De Marco, J. Ware, Z. M. Ruggeri, *J. Biol. Chem.* **1995,** *270*, 9571–9578.
[55] C. Sassetti, K. Tangemann, M. S. Singer, D. B. Kershaw, S. D. Rosen. *J. Exp. Med.* **1998,** *187*, 1965–1975.
[56] K. Hedman, S. Johansson, T. Vartio, L. Kjellen, A. Vaheri, M. Hook. *Cell* **1982,** *28*, 663–671.
[57] A Jukkola, J. Risteli, O. Niemelä, L. Risteli, *Eur. J. Biochem.* **1986,** *154*, 219–224.
[58] D. E. Humphries, J. E. Silbert. *Biochem. Biophys. Res. Co.* **1988,** *154*, 365–371.
[59] P. P. Wilkins, K. L. Moore, R. P. McEver, R. D. Cummings, *J. Biol. Chem.* **1995,** *270*, 22677–22680.
[60] D. Sako, K. M. Comess, K. M. Barone, R. T. Camphausen, D. A. Cumming, G. D. Shaw, *Cell* **1995,** *83*, 323–331.
[61] T. Pouyani, B. Seed, *Cell* **1995,** *83*, 333–343.
[62] P. Rosa, A. Hille, R. W. H. Lee, A. Zanini, P. De Camilli, W. B. Huttner, *J. Biol. Chem.* **1985,** 1999–2011.
[63] F. A. M. Baumeister, V. Herzog, *Cell Tissue Res.* **1988,** *252*, 349–358.
[64] S. Costagliola, V. Panneels, M. Bonomi, J. Koch, M. C. Many, G. Smits, G. Vassart, *EMBO J.* **2002,** *21*, 504–513.
[65] C. B. Fieger, M. C. Huang, J. R. Van Brocklyn, E. J. Goetzl, *FASEB J.* **2005,** *19*, 1926–1928.
[66] C. Surmann-Shmitt, et al., *J. Biol. Chem.* **2008,** *283*, 7082–7093.
[67] D. Jenne, A. Hille, K. K. Stanley, W. B. Huttner, *Eur. J. Biochem.* **1989,** *185*, 391–395.
[68] J. Olsen, et al., *FEBS Lett.* **1988,** *238*, 307–314.
[69] B. Ecarot-Charrier, F. Bouchard, C. Delloye, *J. Biol. Chem.* **1989,** *264*, 20049–20053.
[70] N. Bannert, S. Craig, M. Farzan, D. Sogah, N. V. Santo, H. Choe, J. Sodroski, *J. Exp. Med.* **2001,** *194*, 1661–1673.
[71] J. P. Sleeman, U. Rahmsdorf, A. Steffen, H. Ponta, P. Herrlich, *Eur. J. Biochem.* **1998,** *255*, 74–80.
[72] J. C. Reubl, J.-C. Schaer, B. Waser, *Cancer Res.* **1997,** *57*, 1916–1930.
[73] P. Rosa, A. Hille, R. W. H. Lee, A. Zanini, P. De Camilli, W. B. Huttner, *J. Cell Biol.* **1985,** *101*, 1999–2011.
[74] S. Mortensen, R. T. Kidmose, S. V. Petersen, A. Szilagyi, Z. Prohaszka, G. R. Andersen, *J. Immunol.* **2015,** *194*, 5488–5496.
[75] F. R. Bettelheim, *J. Am. Chem. Soc.* **1954,** *76*, 2838–2839.
[76] D .H. Farrell, E. R. Mulvihill, S. Huang, D. W. Chung, E. W. Davie, *Biochemistry* **1991,** *30*, 9414–9420.
[77] M. C. Liu, F. Lipmann, *Natl. Acad. Sci. USA.* **1985,** *82*, 34–37.
[78] S. C. Huang, D. H. Yu, S. A. Wank, S. Mantey, J. D. Gardner, R. T. Jensen, *Peptides* **1989,** *10*, 785–789.
[79] C. D. Unsworth, J. Hughes, J. S. Morley, *Nature* **1982,** *295*, 519–522.
[80] P. A. Baeuerle, W. B. Huttner, *EMBO J.* **1984,** *3*, 2209–2221.
[81] P. A. Baeuerle, W. B. Huttner, *J. Cell Biol.* **1987,** *105*, 2655–2664.
[82] A. J. Hoffhines, C .H. Jen, J. A. Leary, K .L. Moore, *J. Biol. Chem.* **2009,** *284*, 3096–3105.
[83] M. Paulsson, M. Dziadek, C. Suchanek, W. B. Huttner, R. Timpl, *Biochem. J.* **1985**, *231*, 571–579.
[84] H. U. Yun, H. T. Keutmann, B. A. Eipper, *J. Biol. Chem.* **1994,** *269*, 10946–10955.
[85] L .Paquet, F. Bergeron, A. Boudreault, N. G. Seidah, M. Chrétien, M. Mbikay, C. Lazure, *J. Biol. Chem.* **1994,** *269*, 9276–19285.
[86] D. Cauvi, N. Venot, M. C. Nlend, O. M. Chabaud, *Can. J. Physiol. Pharmacol.* **2003,** *81*, 1131–1138.
[87] M. W. Szkudlinski, V. Fremont, C. Ronin, B. D. Weintraub, *Physiol. Rev.* **2002,** *82*, 473–502.
[88] S. U. Gorr, D. V. Cohn, *J. Biol. Chem.* **1990**, *265*, 3012–3016.
[89] T. Morita, C. M. Jackson, *J. Biol. Chem.* **1986,** *261*, 4008–4014.
[90] G. L. Rosenquist, H. B. Nicholas Jr., *Protein Sci.* **1993**, *2*, 215–222.
[91] S. Hirose, K. Oda, Y. Ikehara, *J. Biol. Chem.* **1988,** *263*, 7426–7430.
[92] P. Antonsson, D. Heinegård, A. Oldberg, *J. Biol. Chem.* **1991,** *266*, 16859–16861.
[93] M. D. Erion, J. Tan, M. Wong, A. Y. Jeng, *J. Med. Chem.* **1994,** *37*, 4430–4437.
[94] N. Charha, R. Kohli, G. L. Kumari, *Mol. Cell. Biochem.* **1991,** *105*, 61–71.
[95] A. Bateman, S. Solomon, H. P. J. Bennett, *J. Biol. Chem.* **1990,** *265*, 22130–22136.
[96] A. Anastasi, G. Bertaccini, V. Erspamer, *Br. J. Pharmocol.* **1966**, *27*, 479–485.
[97] G. Seethaler, M. Chaminade, R. Vlasak, M. Ericsson, G. Griffiths, O. Toffoletto, J. Rossier, H. G. Stunnenberg, G. Kreil. *J. Cell Biol.* **1991,**

114, 1125–1133.
[98] A. Anastasi, V. Erspamer, R. Endean, *Arch. Biochem. Biophys.* **1968,** *125*, 57–68.
[99] L. R. Johnson, G. F. Stening, M. I. Grossman, *Gastroenterology* **1970,** *58*, 208–216.
[100] C. Niehrs, M. Kraft, R. W. H. Lee, W. B. Huttner, *J. Biol. Chem.* **1990**, *265*, 8525-8532.
[101] D. R. Cool, Y. Peng Loh, *Biochimie.* **1994,** *76*, 265–270.
[102] P. Rosa, A. Hille, R. W. Lee, A. Zanini, P. De Camilli, W. B. Huttner, *J. Cell. Biol.* **1985**, *101*, 1999–2011.
[103] S. W. Cha, E. Tadjuidje, J. White, J. Wells, C. Mayhew, C. Wylie, J. Heasman, *Curr. Biol.* **2009,** *19*, 1573–1580.
[104] R. Kumarasamy, D. V. Cohn, *J. Biol. Chem.* **1986,** *261*, 16473–16477.
[105] P. J. Lenting, J. A. van Mourik, K. Mertens, *Blood* **1998,** *92*, 3983–3996.
[106] C. Niehrs, W. B. Huttner, *EMBO J.* **1990,** *9*, 35–42.
[107] D. C. Sane, T. L. Moser, C. J. Parker, D. Seiffert, D. J. Loskutoff, C. S. Greenberg, *J. Biol. Chem.* **1990,** *25*, 3543–3548.
[108] O. Noren, E. Dabelteen, P. E. Hoyer, J. Olsen, H. Sjostrom, G. H. Hansen, *FEBS Lett.* **1989,** *259*, 107–112.
[109] F. Dol, C. Caranobe, D. Dupouy, M. Petitou, J. C. Lormeau, J. Choay, P. Sie, B. Boneu, *Thrombosis Res.* **1988**, *52*, 153–164.
[110] M. C. Kenney, L. M. Shih, U. Labermeir, D. Satterfield, *Biochem. Biophys. Acta.* **1986,** *889*, 156–162.
[111] Z.-W. Fan, J. Eng, M. Miedel, J. D. Hulmes, Y.-C. E. Pan, R. S. Yalow, *Brain Res. Bull.* **1987**, *18*, 757–760.
[112] L. I. Fessler, S. Brosh, S. Chapin, J. H. Fessler, *J. Biol. Chem.* **1986**, *261*, 5034–5040
[113] R. Kohli, N. Chadha, K. Muralidhar, *FEBS Lett.* **1988,** *242*, 139–143.
[114] R. Nichols, S. A. Schneuwly, J. E. Dixon, *J. Biol. Chem.* **1988,** *263*, 12167–12170.
[115] T. M. Kubiak, M. J. Larsen, K. J. Burton, C. A. Bannow, R. A. Martin, M. R. Zantello, D. E. Lowery, *Biochem. Biophys. Res. Co.* **2002,** *291*, 313–320.
[116] K. Broadie, S. Baumagrtner, A. Prokop, *Dev. Neurobiol.* **2011,** *71*, 1102–1130.
[117] P. A. Baeuerle, and W. B. Huttner, *J. Biol. Chem.* **1985,** *260*, 6434–6439.
[118] P. A. Baeuerle, F. Lottspeich, W. B. Huttner, *J. Biol. Chem.* **1988,** *263*, 14925–14929.
[119] H. Duve, A. Thrope, A. G. Scoot, A. H. Johnsen, J. F. Rehfeld, E. Hines, P. D. East, *Eur. J. Biochem.* **1995,** *232*, 633–640.
[120] R. J. Nachman, G. M. Holman, W. F. Haddon, N. Ling, *Science* **1986,** *234*, 71–73.
[121] R. J. Nachman, G. M. Holman, B. J. Cook, W. F. Haddon, N. Ling, *Biochem. Biophys. Res. Co.* **1986,** *140*, 357–364.
[122] A. H. Johnsen, J. F. Rehfeld, *J. Biol. Chem.* **1990,** *265*, 3054–3058.
[123] T. H. Kim, D. H. Kim, H. W. Nam, S. Y. Park, J. Shim, J. W. Cho, *Mol. Cells.* **2010,** *29*, 413–418.
[124] Y. Matsubayashi, Y. Sakagami, *Natl. Acad. Sci. USA.* **1996,** *93*, 7623–7627.
[125] H. Yang, Y. Matsubayashi, K. Nakamura, Y. Sakagami, *Natl. Acad. Sci. USA*. **1999,** *96*, 13560–13565.
[126] Y. Matsubayashi, L. Takagi, N. Omura, A. Morita, Y. Sakagami, *Plant Physiol.* **1999,** *120*, 1043–1048.
[127] Y. Matsuzaki, M. Ogawa-Ohnishi, A. Mori, Y. Matsubayashi, *Science* **2010,** *329*, 1065–1067.
[128] Y. Amano, H. Tsubouchi, H. Shinohara, M. Ogawa, Y. Matsubayashi, *Proc. Natl. Acad. Sci. USA.* **2007,** *104*, 18333–18338.
[129] D. Bagdy, E. Barabas, L. Gráf, T. E. Petersen, S. Magnusson, *Meth. Enzymol.* **1976,** *45*, 669–678.
[130] S. R. Stone, J. Hofsteenge, *Biochemistry* **1986,** *25*, 4622–4628.
[131] M. Loughnan, et al., *J. Biol. Chem.* **1998,** *273*, 15667–15674.
[132] J. L. Wolfender, F. Chu, H. Ball, F. Wolfender, M. Fainzilber, M. A. Baldwin, A. L. Burlingame, *J. Mass Spectrom.* **1999**, *34*, 447–454.
[133] O. Popescu, R. Interior, G. Misevic, M. M. Burger, W. J. Kuhns, *Biol. Bull.* **1999,** *197*, 279–281.
[134] S. Wenzl, M. Sumper, *Dev. Biol.* **1986,** *115*, 119–128.
[135] Z. Yao, W. Jackson, B. Forghani, C. Grose, *J. Virol.* **1993,** *67*, 305–314.
[136] H. Feng, Z. Sun, M. R. Farzan, P. Feng, *J. Virol.* **2010,** *84*, 3351–3361.
[137] J. W. Ludlow, R. A. Consigli, *J. Virol.* **1987,** *61*, 1708–1711.