SUPPLEMENTARY DATA

PrimaryScore from PatternLab and -10lgP from PEAKS are metrics to compare experimental and theoretical spectrum.

Supplementary Table 1: Residues of lysozyme resolved by crystallography and MS and/or phylogenetic analysis

		Crystallography			MS	ConSurf	
Res#	ResType	RSCC	ΔCont	RSCC*	PrimaryScore	n	%
1	K	92.2	9.3	94		173	95.6
3	F	94	4	92.2		93	36.2
4	G	90.9	24.3	94.7		37	13.7
5	R	92.9	3.3	91.5		211	76.7
6	C	94.5	21.7	95.2	1.73	275	98.9
9	A	90.3	5.7	93.4	1.73	242	86.7
10	A	92.3	12.4	92.6	1.73	5	1.8
11	A	85.2	3.2	93	1.73	24	8.6
12	M	95.9	3.3	92	1.73	22	7.9
13	K	89.2	5.8	88.4	1.73	87	31.3
14	R	89.3	4.2	88.8	1.12	74	26.4
16	G	77.6	20.1	91.9	2.02	190	69.6
20	Y	93.7	7.7	94.3	2.02	91	55.8
22	G	83	11.5	91.2	2.71	152	54.1
23	Y	95.3	7	94.2	2.71	79	27.9
24	S	92.8	7.4	94	2.71	133	46.8
26	G	94	9.7	93.7	2.71	37	12.9
28	W	95.1	7.2	93	2.71	273	94.8
30	C	97.1	12	94.1	2.71	295	99.7
31	A	90.1	11.2	94.3	2.71	1	0.3
32	A	93	9.1	95.4	2.71	201	67.9
33	K	91.2	7.4	95.1	2.71	43	14.5
38	F	95	5.4	94.3	2.44	142	48.0
42	A	94.5	8.4	96.8	2.44	206	69.4
43	T	95.1	5.2	95.5	2.44	52	17.5
45	R	92.4	4.9	93.9	2.65	53	18.0
49	G	80.2	29	90.5	3.27	213	72.2
50	S	94.4	8.1	94.1	3.27	252	85.1
53	Y	95.5	5.5	93.4	3.27	198	66.7
54	G	92	15.6	94.9	3.27	294	98.7
58	I	85.5	3.7	91.6	3.27	279	93.6
60	S	94.1	5.7	92.9	3.27	162	54.5
62	W	92	6.4	90.3	1.35	48	16.3
63	W	93	8.7	93.3	1.35	292	99.0
64	C	97.2	12.7	92.6	1.35	297	99.7
67	G	83	14.1	94.4	1.35	130	44.5
68	R	94.1	9.4	90.9	1.35	39	13.3
71	G	67.3	16.2	85.8	2.15	27	19.3
72	S	79.9	3.3	79	2.15	87	31.0
73	R	76.3	**2**	67.8	2.15	13	4.6
76	C	95.4	13.4	91.8	3.85	296	99.3
79	P	91.4	12.9	91.9	3.85	45	15.1

80	C	96.9	13.8	94.3	3.85	296	99.3
82	A	90.5	12.2	94.3	3.85	64	22.1
84	L	91.3	5.3	94.1	3.85	199	70.6
89	T	90	4.2	93.5	3.85	100	36.0
90	A	87.1	13.7	95.9	3.85	24	8.6
94	C	96.3	16.5	91.4	3.85	278	99.6
95	A	90.4	10.1	94.7	3.85	216	77.7
96	K	91.7	5	93.5	3.85	196	70.5
98	I	94.2	7.5	94.8	3.39	201	72.3
100	S	91.1	7.8	90.3	3.39	42	15.2
102	G	78.2	18.9	89.8	3.39	1	0.4
104	G	85.4	9.2	94.1	3.39	259	93.8
105	M	95.8	3.3	94.6	3.39	70	25.4
107	A	89.2	16.1	91.8	3.39	199	72.1
108	W	94.7	12.6	91.7	3.39	273	99.3
110	A	93.8	11.7	93.8	3.39	95	35.1
111	W	95.9	12.7	91.9	3.39	205	74.5
114	R	91.4	4.6	90.2	1.07	22	8.1
115	C	95.9	10.6	91.3	1.07	265	98.9
116	K	94.5	11	95.2	1.07	62	23.4
118	T	95.5	5.1	93.8	1.67	12	5.3
120	V	94.6	3.6	93.3	1.67	18	11.4
122	A	86.4	8.2	89.4	1.67	5	3.0
123	W	93.4	13.8	91.2	1.67	79	47.3
126	G	78.7	26.1	88.4	1.67	130	81.2
127	C	94	12.7	92.5	1.20	159	99.4

Res# stands for residue number; ResType for residues type; RSCC for real-space correlation coefficient; ΔCont for minimum difference within other RSCC; * for main chain atoms; MS for mass spectrometry. RSCC in bold denotes cysteine partially occupied having ΔCont less than 3.0.

Supplementary Table 2: Residues of lysozyme having assignment ambiguity from crystallographic data being resolved by mass spectrometry

		Crystallography			MS	ConSurf	
Res#	ResType	RSCC	ΔCont	Observation	PrimaryScore	n	%
7	E!	93.5	0.6		1.73	167	59.9
7	Q	93	5.8			12	4.3
7	MainCh	94.6					
8	L!	92.5	1	Hydrophobic	1.73	215	77.1
8	N	91.5	0.5			0	0.0
8	D	91	7.5			0	0.0
8	MainCh	93.7					
15	H!	93.5	2.1		2.02	60	22.1
15	F	91.4	0.5			20	7.4
15	K	90.9	2.1			6	2.2
15	MainCh	93.4					
17	D	91.3	0.2			0	0.0

17	N	91.1	2			0	0.0
17	L!	89.1	8.1	Hydrophobic	2.02	110	39.3
17	MainCh	88.4					
18	N	91.3	0.7	2 H-bonds		12	7.1
18	D!	90.6	1		2.02	120	71.4
18	L	89.6	7.6			0	0.0
18	MainCh	93.5					
25	L!	91.5	1.9	Hydrophobic	2.71	198	69.2
25	N	89.6	0.6			0	0.0
25	D	89	7.1			0	0.0
25	MainCh	92.3					
29	V!	95.5	1.1	Hydrophobic	2.78	160	54.1
29	T	94.5	4.1			18	6.1
29	MainCh	91.4					
34	F!	95.7	2.3		2.44	39	13.2
34	H	93.5	3.6			97	32.8
34	MainCh	94.8					
35	E!	94.2	1.2		2.44	248	83.8
35	Q	93	4.2			3	1.0
35	MainCh	94.7					
36	S!	92.7	1.2		2.44	290	98.0
36	C	91.5	10.1			0	0.0
36	MainCh	93.5					
39	N!	94.5	1.5	4 H-bonds	2.44	208	70.3
39	D	93	1.2			48	16.2
39	L	91.8	7.1			0	0.0
39	MainCh	94.5					
40	T!	91.1	0.7	3 H-bonds	2.44	249	84.1
40	V	90.4	3.6			2	0.7
40	MainCh	95.1					
44	N!	92.9	2.8	4 H-bonds	2.44	106	35.9
44	L	90.1	0.1			0	0.0
44	D	90	6.8			20	6.8
44	MainCh	96					
47	V	86.2	4.6	3 H-bonds		10	3.6
47	T!	81.7	1.2		3.27	31	11.0
47	MainCh	85.9					
51	T!	95.5	1.5	2 H-bonds	3.27	118	39.9
51	V	94	5.4			8	2.7

51	MainCh	94.3					
55	V	90.4	1.3	Hydrophobic		2	0.7
55	T	89.1	4.8			0	0.0
55	S	84.3	0			0	0.0
55	I!	84.3	4.5		3.28	179	60.1
55	MainCh	93.2					
56	N	91	0.8	Hydrophobic		0	0.0
56	D	90.2	2.3			0	0.0
56	L!	88	4.3		3.28	10	3.4
56	MainCh	91.6					
61	S	84.6	1.6			6	2.0
61	R!	83	2.8		3.28	111	37.2
61	MainCh	87.7					
65	D	95.1	0.8	2 H-bonds		41	13.8
65	N!	94.3	1.9		1.35	75	25.3
65	L	92.5	2.8			0	0.0
65	MainCh	94.8					
69	S	93.2	0.2	4 H-bonds		27	13.9
69	T!	93	2		2.15	66	34.0
69	C	91	7.2			0	0.0
69	MainCh	93.8					
74	D	93.9	2.9	3 H-bonds	2.69	11	3.7
74	N!	90.9	0.8		3.85	202	67.8
74	MainCh	74.5					
75	L!	92.1	0.5	Exposed	3.85	40	13.4
75	S	91.6	3.8		2.15	2	0.7
75	MainCh	90.6					
77	A	82.5	3		2.15	1	0.3
77	V	79.5	0.4			1	0.3
77	S	79.1	1.1		2.00	8	2.7
77	I	78	1			0	0.0
77	L	76.9	1.1			0	0.0
77	N!	75.8	0.3		3.85	75	25.2
77	MainCh	93.3					
78	T	90.3	1.2	Hydrophobic		12	4.0
78	V	89.1	0.2		2.00	82	27.5
78	I!	88.9	6.4		3.85	116	38.9
78	MainCh	91.5					
81	S!	91.3	2.5		3.85	117	39.3
81	T	88.8	2.7		2.15	15	5.0

81	MainCh	92.8					
83	L!	90.5	2.8	Hydrophobic	3.85	222	77.9
83	N	87.7	1.3			0	0.0
83	D	86.4	5.5			0	0.0
83	MainCh	93.5					
88	I!	92.2	2.6		3.85	181	65.1
88	V	89.6	0.8			11	4.0
88	MainCh	95.5					
91	S!	87.6	1.3	2 H-bonds	3.85	41	14.7
91	T	86.3	2.7		1.87	27	9.7
91	MainCh	91.8					
92	I	87.9	0.4			126	45.2
92	T	87.5	0.1			4	1.4
92	V!	87.4	7.3		3.85	112	40.1
92	MainCh	92.3					
99	V!	92.3	0.6	Hydrophobic	3.39	118	42.6
99	T	91.7	5.2			3	1.1
99	MainCh	95.4					
106	D	93.9	0.5	3 H-bonds	1.97	21	7.6
106	N!	93.4	1.5		3.39	56	20.3
106	L	91.9	0.8			1	0.4
106	E	91.1	9.1			7	2.5
106	MainCh	93.5					
109	T	85.8	0.8	Exposed	1.15	36	13.3
109	V!	85	0.9		3.39	73	26.9
109	S	84.1	3.6			19	7.0
109	MainCh	92.2					
112	R!	86.9	0.9		3.39	68	25.5
112	K	86.1	1			82	30.7
112	S	85	2.4			14	5.2
112	MainCh	91.7					
117	G!	64.2	0.3		1.67	139	54.5
117	K	63.9	8.6			3	1.2
117	MainCh	89.6					
124	T	92.6	2.1	Exposed		18	11.0
124	V	90.5	2.1		1.34	56	34.4
124	I!	88.4	4.7		1.67	32	19.6
124	MainCh	93.7					
125	A	83.4	4.3			20	12.5

125	G	79.2	2.2		0.82	1	0.6
125	S	76.9	4.8		0.90	9	5.6
125	K	72.2	1.7		1.34	27	16.9
125	R!	70.5	0.5		1.67	25	15.6
125	MainCh	91.4					
129	N	81.1	0.4	Hydrophobic		0	0.0
129	D	80.7	0.4			0	0.0
129	L!	80.2	2.8		1.07	70	97.2
129	MainCh	71.1					

Res# stands for residue number; ResType for residues type; RSCC for real-space correlation coefficient; ΔCont for minimum difference within other RSCC; MainCh for main chain atoms; MS for mass spectrometry; H-bond for hydrogen bond; ! for resolved residue.

Supplementary Table 3: Residues of lysozyme having ambiguity assignment from both crystallographic and mass spectrometry data but being resolved by phylogenetic analysis

		Crystallography			MS	ConSurf	
Res#	ResType	RSCC	ΔCont	Observation	PrimaryScore	n	%
2	V!	92.5	2.3	Exposed		104	47.5
2	T	90.2	5.5			20	9.1
2	MainCh	94.6					
19	S	85	3.6			1	0.6
19	A	81.4	2.4			0	0.0
19	V	79	1.4			0	0.0
19	L	77.6	0.7			1	0.6
19	I	76.9	0.3			0	0.0
19	K	76.6	1.7			4	2.5
19	G	74.9	0.1			124	76.5
19	T	74.8	1.3			1	0.6
19	N!	73.5	2.1		1.88	14	8.6
19	D	71.4	1		2.02	2	1.2
19	MainCh	91.8					
21	K	83.1	1.7		2.40	17	6.1
21	A	81.4	0.5			8	2.9
21	R!	80.9	3.1		2.71	58	20.8
21	MainCh	95.7					
27	N!	95.6	0.6	4 H-bonds	2.78	122	42.4
27	D	95	3.4		2.55	72	25.0
27	MainCh	93.8					
37	N!	93.1	0.6	1 H-bonds	2.44	55	18.6
37	D	92.5	1.3		2.13	14	4.7
37	L	91.2	4.4			2	0.7
37	MainCh	94.7					
41	E	95.4	1.3		1.95	5	1.7
41	Q!	94.1	3.2		2.44	35	11.8

41	MainCh	93.5					
46	D	94.6	1.3	3 H-bonds	3.27	0	0.0
46	N!	93.3	2.5		3.11	106	41.9
46	MainCh	88.8					
48	D!	96.2	0.3	5 H-bonds	3.27	178	62.0
48	N	96	9.6		2.63	53	18.5
48	MainCh	93.8					
52	D!	93.8	0.9	5 H-bonds	3.28	212	71.1
52	N	92.9	6.1		3.01	32	10.7
52	MainCh	96.6					
57	E	91.1	0.2		1.44	1	0.3
57	Q!	90.9	5		1.32	293	98.3
57	MainCh	93.9					
59	N!	85.1	0.1	4 H-bonds	3.28	207	69.5
59	M	84.9	2.3			0	0.0
59	D	82.6	0.4		3.12	2	0.7
59	MainCh	90.7					
66	D!	95.6	1.4	8 H-bonds	1.00	110	37.2
66	N	94.3	8.2		0.60	45	15.2
66	MainCh	96.2					
85	T!	89.6	2		2.98	45	16.4
85	S	87.6	3		3.85	35	12.7
85	MainCh	91.1					
86	A	84.1	3.7	2 H-bonds	2.00	6	2.2
86	V	80.4	0.6			1	0.4
86	S!	79.8	3.9		3.85	30	10.8
86	T	75.8	1.4		1.88	2	0.7
86	MainCh	91.3					
87	D!	91.7	0.1	2 H-bonds	3.85	179	64.4
87	N	91.6	1.4		2.94	76	27.3
87	Q	90.3	4.4			0	0.0
87	MainCh	94.2					
93	N!	91.8	2.9	1 H-bonds	3.85	24	8.6
93	D	88.9	1		3.56	4	1.4
93	MainCh	93					
97	A	83.4	2.8			1	0.4
97	K!	80.7	0.2		2.92	107	38.5
97	MainCh	94.1					

101	N	92.9	1	1 H-bonds	3.39	4	2.9
101	D!	91.9	1		3.09	60	43.8
101	L	90.9	6.8			0	0.0
101	MainCh	91.2					
103	N	88	1.3	1 H-bonds	2.91	24	8.7
103	L	86.7	0.9			2	0.7
103	D!	85.9	6.6		3.39	9	3.3
103	MainCh	94.4					
113	N!	96.2	2.4	2 H-bonds	1.07	61	24.0
113	D	93.8	1.2			7	2.8
113	MainCh	91.3					
119	D!	91.5	1.6	2 H-bonds	1.67	102	50.7
119	N	90	0.9		1.07	29	14.4
119	L	89.1	7			0	0.0
119	MainCh	92.3					

Res# stands for residue number; ResType for residues type; RSCC for real-space correlation coefficient; ΔCont for contrast difference within other RSCC; MainCh for main chain atoms; MS for mass spectrometry; H-bond for hydrogen bond; ! for resolved residue.

Supplementary Table 4: Residues of lysozyme having ambiguity assignment from both crystallographic and mass spectrometry data but being resolved by intact mass MS measurement.

		Crystallography			MS	ConSurf	
Res#	ResType	RSCC	ΔCont	Observation	PrimaryScore	n	%
70	G	79.8	3		2.15	7	3.7
70	P!	76.8	3			81	42.9
70	A	73.8	8.7			3	1.6
70	MainCh	87					
121	S	87.3	6.5		1.59	103	57.9
121	L	80.8	0.0		0.50	1	0.6
121	A	80.8	0.9		1.67	11	6.2
121	G	79.9	1.7		0.90	2	1.1
121	N	78.2	0.4		1.34	7	3.9
121	V	77.8	2.3			1	0.6
121	C	75.5	2.5			0	0.0
121	K	73.0	1.0			4	2.2
121	D	72.0	3.9			12	6.7
121	T	68.1	0.7			17	9.6
121	I	67.4	2.0			1	0.6
121	Y	65.4	1.1			2	1.1
121	E	64.3	1.8			5	2.8
121	H	62.5	1.2			0	0.0
121	R	61.3	2.4			5	2.8
121	P	58.9	4.9			3	1.7
121	Q!	54.0	1.3			2	1.1
121	MainCh	91.8					

128	S	88.2	2.6		0	0.0
128	T	85.6	1.4		2	1.6
128	V	84.2	1.3	0.82	0	0.0
128	A	82.8	5		0	0.0
128	D	77.8	2.7	0.90	20	16.1
128	P	75.1	0.5	1.07	0	0.0
128	L	74.6	2.5		0	0.0
128	I	72.1	2.1		0	0.0
128	N	70	1.1	1.64	15	12.1
128	C	68.9	8.4		0	0.0
128	R!	50.5			13	10.5
128	MainCh	79.4				

Supplementary Table 5: Residues of the basement membrane-specific heparan sulphate proteoglycan core protein (BaM) resolved by crystallography, MS and/or phylogenetic analysis

		Crystallography			MS Score		ConSurf	
Res#	ResType	RSCC	ΔCont	RSCC*	PrimaryScore	-10lgP	n	%
1769	P	90.6	8.5	87.5	5.21		88	89.8
1770	I	93.7	5	95	5.21		33	75
1771	M	84.4	1.1	94.3	5.21		2	2.6
1772	V	92.2	0.6	94.7	5.21		46	38.7
1773	T	89.8	1	94.8	5.21		16	12.5
1774	V	92.4	4.2	96	5.21		30	22.4
1775	E	83.9	2.3	91.8	5.21		25	17.9
1776	E	71.2	3.8	78.4	5.21		48	30.8
1777	Q	48.5	2.7	71.8	5.21		9	5.1
1778	R	70.4	0.7	91.9	5.21		30	15.8
1779	S	62.7	4	91.1		19.15	60	28.8
1780	Q	95.7	0.1	93.7		19.15	74	32.7
1781	S	88.3	2.2	95.5		19.15	49	19.3
1782	V	94.7	2.1	96.2		19.15	183	69.1
1783	R	46.2	0.9	91.9		19.15	61	22.8
1784	P	91.8	11.2	96		19.15	57	20.5
1785	G	76	28.5	91.1		19.15	261	91.3
1786	A	78.3	3.3	92.5		19.15	41	14.2
1787	D	92.5	4.7	94.5		19.15	59	20.3
1788	V	90.9	0.5	95.2		19.15	174	59.2
1789	T	92.1	0.5	94.8		19.15	93	31.6
1790	F	93.4	4.6	95.3		19.15	138	46.9
1791	I	90.8	0.4	96		19.15	25	8.5
1792	C	82.1	6.5	91.8		19.15	298	100
1793	T	92.6	9	94.5		19.15	54	18.1
1794	A	89.2	12	95.4		19.15	185	61.9
1795	K	83.7	0.7	95.1		19.15	31	10.4
1796	S	94.3	5.7	94.9		19.15	50	16.9
1799	P	91.1	11.6	94.5			225	75
1802	T	96.5	8.1	96			121	40.3
1805	W	97.1	12.8	95.8			299	99.7
1811	G	86.4	8.1	95			160	53.7
1813	L	95.4	7.5	94			237	80.1

1822	G	90.3	6.7	95		228	76
1824	L	95.2	4.4	94.3		275	91.7
1831	P	92.2	15.6	95.2		117	39
1833	D	95.2	3.7	94		259	86.3
1835	G	88.4	30.5	92.3		291	97
1837	Y	95.7	8.7	95.2		297	99
1839	C	96.5	15.3	95.4		300	100

Res# stands for residue number; ResType for residues type; RSCC for real-space correlation coefficient; * for main chain atoms; MS for mass spectrometry.

Supplementary Table 6: Residues of BaM having assignment ambiguity from phylogenetic analysis being resolved by crystallographic data

		Crystallography		ConSurf	
Res#	ResType	RSCC	Observation	n	%
1798	S!	84.5		13	50
1798	R	53.5		3	11.5
1798	MainCh	94.8			
1800	A!	97.2		49	16.4
1800	T	68.9		38	12.7
1800	P	58.3		65	21.7
1800	MainCh	96.4			
1801	Y!	96.4		29	9.7
1801	P	58.6		182	60.9
1801	MainCh	95.4			
1803	L!	95.5	hydrophobic	99	33
1803	I	81.8		78	26
1803	V	74.6		74	24.7
1803	MainCh	95.6			
1804	V!	96.1	hydrophobic	45	15
1804	T	94.7		87	29
1804	S	87.1		43	14.3
1804	MainCh	96			
1806	T!	94.4	hydrophilic	106	35.3
1806	S	89.3		74	24.7
1806	R	49.9		28	9.3
1806	MainCh	94.3			
1807	R!	91.5		146	48.7
1807	K	84		112	37.3
1807	MainCh	92.4			
1808	L!	87.2		50	16.7
1808	V	80.9		39	13
1808	N	73.8		30	10

1808	E	62		32	10.7
1808	MainCh	93.9			
1814	P!	91		226	75.6
1814	S	56.7		28	9.4
1814	MainCh	93.7			
1815	S!	86.2		70	23.4
1815	A	75.5		28	9.4
1815	P	62		39	13
1815	MainCh	93.3			
1816	R!	93.3		72	24.3
1816	S	82.2		42	14.2
1816	G	71.7		35	11.8
1816	N	63.5		39	13.2
1816	MainCh	95.2			
1817	A!	94.3		128	43.2
1817	S	75.5		49	16.6
1817	R	18.5		37	12.5
1817	MainCh	92.9			
1819	D!	95.8	hydrophilic	41	13.9
1819	N	94.5		2	0.7
1819	L	90.4		36	12.2
1819	I	77.8		42	14.3
1819	V	59.1		86	29.3
1819	MainCh	95.2			
1821	N!	91.9	hydrophilic	92	30.7
1821	D	89		38	12.7
1821	G	60.4		87	29
1821	MainCh	95.2			
1823	I!	94.4		50	16.7
1823	T	88.4		55	18.3
1823	V	86.5		48	16
1823	S	84.4		36	12
1823	MainCh	93.6			
1825	T!	93.4	hydrophilic	139	46.5
1825	R	63.4		30	10
1825	MainCh	93.5			
1826	I!	93		225	75
1826	L	80.7		43	14.3
1826	MainCh	93			
1827	S	82.7		19	6.3

1827	K	79.5		9	3
1827	R!	73.8		72	24
1827	P	55.1		64	21.3
1827	MainCh	92.6			
1828	N!	92.1	hydrophilic	118	39.6
1828	D	90.7		23	7.7
1828	S	75.5		33	11.1
1828	A	66.4		30	10.1
1828	MainCh	94.5			
1829	V!	94.8	hydrophobic	186	62
1829	I	91.6		29	9.7
1829	A	74.6		51	17
1829	MainCh	95.8			
1830	Q!	93.8	hydrophilic	73	24.3
1830	E	91.2		12	4
1830	S	82.8		32	10.7
1830	R	67.8		38	12.7
1830	T	63.2		63	21
1830	MainCh	95.6			
1832	S!	92.8		80	26.7
1832	E	65.7		85	28.3
1832	MainCh	95.6			
1834	A!	91.6		141	47
1834	S	78.9		61	20.3
1834	MainCh	94.3			
1836	T!	90.6	hydrophilic	78	26
1836	V	88.6		31	10.3
1836	I	82.5		29	9.7
1836	Q	38.1		29	9.7
1836	MainCh	93			
1840	T!	95.7	hydrophilic	148	49.3
1840	V	90.7		38	12.7
1840	MainCh	96.2			
1841	G!	94.7		45	15.3
1841	A	75.9		217	73.6
1841	MainCh	95			
1845	H	85.2		12	5
1845	F!	84.8		27	11.3
1845	A	73.9		43	18
1845	V	59.1		50	20.9
1845	MainCh	93.8			

1847	M!	83		24	11.6
1847	A	82.2		9	4.3
1847	S	81.2		32	15.5
1847	T	74		38	18.4
1847	MainCh	92.7			
1848	D!	93.8	hydrophilic	63	31.7
1848	N	92.9		5	2.5
1848	S	76.7		21	10.6
1848	A	68		34	17.1
1848	V	60.4		34	17.1
1848	MainCh	95.2			
1850	G!	88.7		33	17.6
1850	A	78.7		50	26.6
1850	S	47.3		26	13.8
1850	MainCh	94.2			
1851	T!	94.5	hydrophilic	69	38.3
1851	R	57.5		22	12.2
1851	MainCh	94.2			
1852	A!	93.6		85	47.8
1852	V	72.1		38	21.3
1852	MainCh	94.8			
1854	L!	94.2	hydrophobic	136	84.5
1854	V	71.8		16	9.9
1854	MainCh	94			
1855	H!	89.4		28	20
1855	N	78.5		14	10
1855	Y	72.6		17	12.1
1855	S	69.3		14	10
1855	R	56.6		16	11.4
1855	MainCh	95.4			
1856	V!	90.8	hydrophobic	109	83.8
1856	I	85.4		17	13.1
1856	MainCh	94.8			

Res# stands for residue number; ResType for residues type; RSCC for real-space correlation coefficient; ΔCont for minimum difference within other RSCC; MainCh for main chain atoms; H-bond for hydrogen bond; ! for resolved residue.

Supplementary Table 7: Residues of BaM having ambiguity assignment from crystallographic, and mass spectrometry and phylogenetic data

		Crystallography		ConSurf	
Res#	ResType	RSCC	Observation	n	%
1797	S	85.1		39	13.2

1797	K!	82.6		27	9.2
1797	N	78.5		34	11.5
1797	MainCh	90.6			
1809	H!	91.7		3	2.7
1809	N	77.6		12	10.6
1809	D	77.4		29	25.7
1809	S	68.2		14	12.4
1809	G	56.6		26	23
1809	MainCh	93.4			
1810	N!	95.1	hydrophilic	64	21.3
1810	D	92.3		37	12.3
1810	G	62.5		96	32
1810	MainCh	96			
1812	S	88.9		30	10.1
1812	K!	83.8		25	8.4
1812	A	71.1		32	10.7
1812	P	51.9		61	20.5
1812	MainCh	94.4			
1818	A	88.4		12	4.1
1818	V	81.4		47	15.9
1818	T	77.2		28	9.5
1818	Q	75.8		30	10.1
1818	M!	71		20	6.8
1818	R	66.8		49	16.6
1818	MainCh	92.9			
1820	F!	94.8		22	7.4
1820	K	83.1		31	10.4
1820	R	72.4		43	14.4
1820	E	72		29	9.7
1820	MainCh	93.8			
1838	V!	91.5		80	26.7
1838	T	89.6		43	14.3
1838	I	87.7		38	12.7
1838	MainCh	95.4			
1842	S!	88.1	hydrophilic	123	42.3
1842	T	85.9		58	19.9
1842	MainCh	94.3			
1844	A	84.4		22	8
1844	E	79.7		18	6.5
1844	Q	79.2		10	3.6
1844	M!	74.9		21	7.6
1844	S	71.2		33	12

1844	N	53.9	39	14.2
1844	MainCh	91.2		
1846	A!	89.2	15	6.8
1846	G	65.2	163	73.8
1846	MainCh	92.8		
1849	Q!	93.8	42	21.3
1849	E	93.2	51	25.9
1849	T	63	39	19.8
1849	MainCh	95.1		
1853	V	88.9	20	12
1853	T!	86.7	53	31.7
1853	R	54.2	18	10.8
1853	MainCh	92.6		
1857	S	77.4	0	0
1857	E	76.9	7	11.9
1857	Q!	76.1	37	62.7
1857	MainCh	82.3		

Res# stands for residue number; ResType for residues type; RSCC for real-space correlation coefficient; ΔCont for contrast difference within other RSCC; MainCh for main chain atoms; MS for mass spectrometry; H-bond for hydrogen bond; ! for resolved residue.

Supplementary Table 8: Residues of metalloproteinase resolved by crystallography and MS and/or phylogenetic analysis

		Crystallography			MS	ConSurf	
Res#	ResType	RSCC	ΔCont	RSCC*	PrimaryScore	n	%
2	F	92.2	4.0	94.3	1.04	10	76.9
3	S	91.8	5.5	94.3	1.33	26	44.8
4	P	93.7	12.5	97.1	1.33	30	15.9
5	R	96.9	8.2	97.9	1.33	87	33.2
6	Y	97.3	5	98.1	3.03	226	85.3
7	I	96.8	3.8	97.7	3.03	75	28.3
8	E	97.7	4.6	98.3	3.03	247	93.6
10	A	95.2	12.1	97.7	3.03	15	5.7
13	A	95.3	9.9	97.8	3.03	161	60.8
16	G	92	21.3	97.8	3.03	24	9.0
17	M	96.5	4.5	97.9	3.03	67	24.7
18	F	95.6	4.6	96	3.03	140	52.2
20	K	97	9.5	96.8	3.03	149	55.6
21	Y	97.2	7.2	96.5	2.26	115	42.6
23	S	95.7	8.8	97.2	2.36	34	12.6
25	L	93.7	3.3	96.2	2.36	102	39.1
27	T	96.9	3.3	97.3	2.36	50	18.5
28	I	95.2	4	97.3	2.36	81	30.0
31	R	96.9	9.6	96.9	2.08	213	78.3
33	H	93.6	4.4	97.2	2.52	9	3.3

34	E	92.4	5.8	97.5	2.52	206	75.7
35	M	98.6	4.7	98.7	2.52	39	14.3
38	T	97.5	5.6	98.1	2.52	24	8.8
41	G	95.6	21.5	98	2.52	10	3.5
42	F	96.9	6.5	98.4	2.52	108	36.7
43	Y	98.4	6.4	98.5	1.36	257	86.8
44	S	91.5	8.1	97.4	1.36	4	1.4
45	S	96.6	11.6	97.8	1.36	33	11.1
48	A	97	11.1	98.2	1.36	2	0.7
50	A	94.4	13.9	95.4	1.36	4	1.3
51	S	97.1	7.5	97	1.36	9	3.0
52	L	97	4.6	97.4	1.36	291	98.0
53	A	96	8.4	98.2	1.36	5	1.7
54	N	96.9	3	97.5	1.36	4	1.3
58	W	98.3	12.2	97.8	1.36	294	99.0
59	S	95.8	7.8	96.5	1.36	146	49.2
63	L	97.1	3	97.6	1.82	43	14.5
64	I	96.7	6.9	97.9	1.82	171	57.6
68	K	95.3	10	98.1	1.82	16	5.4
70	S	97.6	7.9	98.2	1.65	31	10.4
72	K	93.6	4.6	97.3	1.65	3	1.0
73	T	98.2	4.7	97.6	2.26	256	85.6
74	L	96.9	3.2	98.1	2.26	290	97.0
75	T	96.7	5.7	97.2	2.26	11	3.7
76	S	96.7	8.8	97.3	2.26	79	26.4
77	F	98	8	97.8	2.26	294	98.3
78	G	91.1	29.5	97	2.26	47	15.7
79	S	85.5	4.3	95.7		27	9.0
80	W	98.5	13.6	97.6	2.26	284	95.0
81	R	97.2	10.2	97.8	2.26	276	92.3
83	R	93.2	6	98.1	1.80	42	14.1
87	P	96.2	17	96.4	1.80	107	35.9
88	R	92.9	5.8	98	1.80	211	70.8
90	S	95.6	9.6	98.6	4.59	37	12.4
91	H	97.9	3.8	98.6	4.59	234	78.3
93	H	98.3	3.3	98.8	4.59	10	3.3
94	A	97.2	7.9	98.4	4.59	275	92.0
96	L	97.2	3.7	97.9	4.59	265	89.2
97	L	92.9	3.7	98	4.59	125	42.1
98	T	97.1	4.6	98.4	4.59	220	74.1
99	T	97.3	4.7	98.1	4.59	3	1.0
100	I	94.2	3.9	96.8	4.59	98	33.0
102	F	98.1	4.8	97.5	4.59	264	88.9
103	D	97.7	3.1	97.8	4.59	67	22.6
105	Y	95.4	4.5	97.4	4.59	1	0.3
107	I	96	4.3	98	4.59	118	39.6
108	G	92.8	13.9	98.2	4.59	296	99.3
109	R	96.7	7	98.2	4.59	10	3.4
111	R	94.5	7	97.3	3.04	6	2.0
112	S	93.2	2.9	96.1	1.19	2	0.7

113	G	94.5	10.6	98.2	1.19	79	26.5
114	K	96.6	5.2	98.8	1.19	1	0.3
115	M	98.2	4.4	97.3	1.19	220	73.8
116	C	97.9	10.3	97.9	1.19	298	100.0
118	P	95.5	18.3	97.4	1.19	68	22.9
121	S	98	9.1	98	2.37	293	98.7
123	G	93.6	9.2	98.3	2.37	227	76.7
129	S	96.2	6	97.5	2.37	194	65.5
130	K	86.9	3.3	96.9	2.37	25	8.5
133	L	96.6	4.9	97.9	2.97	102	34.6
134	W	97.6	8	98.7	2.97	1	0.3
136	A	97	15.3	97.8	2.97	266	89.9
139	M	98.7	5.3	98.2	2.97	159	53.7
138	T	97.5	6.4	98.2	2.97	245	82.8
140	A	97	12.7	98	2.97	282	95.3
141	H	97.1	4.8	98.2	2.97	296	100.0
143	L	96.6	3.7	97.4	2.97	121	40.9
144	G	96.5	13.3	98.8	2.97	295	99.7
145	H	98.3	5.7	98.2	2.97	296	100.0
149	M	98.2	4.9	98	2.97	222	75.3
151	H	96.8	5.9	98.5	2.97	292	99.0
155	C	90.7	**2.1**	96.4	2.97	289	98.6
156	S	96.4	8.5	97.3	2.97	32	10.9
157	C	91.9	**1.6**	97.6	2.97	239	87.9
158	G	96.7	15.1	98.6	2.97	53	18.3
159	A	97.7	16.5	98.4	2.97	97	33.9
160	K	95.5	7.5	98.5	2.97	18	6.3
161	S	97.9	9.5	97.7	2.21	58	20.5
162	C	93.2	**2.7**	97.6	2.21	281	98.9
163	I	97.4	8.9	97.6	2.21	198	69.7
164	M	98.8	5.6	98	2.21	280	98.6
165	A	96.8	9.5	98.1	2.21	129	45.6
166	S	95.8	8	96.2	2.21	21	7.4
168	L	97.9	3.4	96.9	2.21	65	24.0
169	S	95.9	10.5	97.3	2.21	85	30.4
170	K	94.9	7.2	97.2	2.21	6	2.2
172	K	92.9	6.5	97.3	2.54	2	0.7
174	Y	97.4	6.1	97.3	2.63	25	9.0
175	A	95.7	13	98.3	2.63	4	1.4
176	F	97.7	5.9	97.8	2.63	265	94.6
177	S	97.2	7.7	98.2	2.63	262	93.6
180	S	96.9	9	97.6	2.63	256	91.8
184	Y	97.4	6.8	97.9	2.63	56	20.2
187	F	96.9	6.5	97	2.63	93	33.8
191	H	94.9	5.4	98.6	1.50	10	3.7
192	N	97.7	3.1	98.2	1.50	30	11.1
193	P	95.7	12.3	97.6	1.50	108	39.9
195	C	91.1	3.5	97.4	1.50	271	100.0
196	I	98	6	98.4	1.50	62	23.0
197	L	95.9	4.2	97.4	1.50	99	37.9

200	P	91.6	16.9	92.8	0.82	246	100.0

Res# stands for residue number; ResType for residues type; RSCC for real-space correlation coefficient; ΔCont for contrast difference within other RSCC; * for main chain atoms; MS for mass spectrometry. RSCC in bold denotes cysteine partially occupied having ΔCont less than 3.0.

Supplementary Table 9: Residues of metalloproteinase having assignment ambiguity from crystallographic data being resolved by mass spectrometry

		Crystallography			MS	ConSurf	
Res#	ResType	RSCC	ΔCont	Observation	PrimaryScore	n	%
1	V	78	1.2	No H-bond			
1	G	76.8	2.6				
1	T!	74.2	0.9		1.04		
1	I	73.3	1.3				
1	A	72	1.4		1.33		
1	L	70.6	0.1				
1	MainCh	88.3					
9	L!	87.7	0.9		3.03	211	79.9
9	V	86.8	0.8			8	3.0
9	S	86	2.1		1.33	0	0.0
9	I	83.9	0.2			2	0.8
9	A	83.7	0.2		1.04	0	0.0
9	MainCh	97.4					
11	V!	97.7	1.6		3.03	64	24.2
11	T	96.1	3.2			0	0.0
11	MainCh	97.4					
12	V!	95.5	1.8		3.03	256	96.6
12	T	93.7	2.4			0	0.0
12	MainCh	97					
14	D!	97.6	1.1	3 H-bonds	3.03	263	99.2
14	N	96.5	4.7		1.33	1	0.4
14	L	91.8	10.2			0	0.0
14	MainCh	97.7					
19	V	94.4	0.7			10	3.7
19	T!	93.7	6.5	2 H-bonds	3.03	22	8.2
19	MainCh	95.7					
22	N!	92.6	2.7		2.36	76	34.7
22	S	89.9	3.8	1 H-bond and exposed residue		17	7.8
22	L	86.1	2.1			0	0.0
22	D	84	3.3		2.08	15	6.8
22	MainCh	96.5					
29	S	90.5	2.2			1	0.4
29	V	88.3	0.2			3	1.1
29	A	88.1	5.9			0	0.0
29	T	82.2	2.2			2	0.7
29	Q	80	1.3			22	8.1
29	L	78.7	0.4			9	3.3
29	I	78.3	0.4			9	3.3
29	E	77.9	1.1		2.08	6	2.2

29	K	76.8	1.6	Double occupancy		101	37.0
29	R!	74.5	2.1	1 H-bond and exposed residue	2.36	103	37.7
29	MainCh	98					
30	T!	95.7	1.7	2 H-bonds	2.08	45	16.5
30	V	94	3.4			4	1.5
30	MainCh	97.3					
32	V!	98.1	1.8	Hydrophobic and buried region	2.52	70	25.7
32	T	96.3	3.2			7	2.6
32	MainCh	97.7					
36	V!	97.2	1.2	Hydrophobic and buried region	2.52	126	46.2
36	T	96	4.5			4	1.5
36	MainCh	98.5					
37	N!	86	0.4		2.52	255	93.8
37	T	85.6	0.2			0	0.0
37	S	85.4	0.2	1 H-bond and exposed residue		6	2.2
37	V	85.2	6.3			0	0.0
37	L	78.9	7.7			4	1.5
37	D	71.2	4.3		1.36	1	0.4
37	MainCh	97.2					
39	V!	96.7	2.5	Hydrophobic and buried region	2.52	174	63.3
39	T	94.2	3.4			0	0.0
39	MainCh	98.8					
40	N!	94.7	1.7	3 H-bonds and exposed residue	2.52	117	42.2
40	L	93	0.1			1	0.4
40	D	92.9	5.4		1.36	146	52.7
40	MainCh	98.1					
46	V!	96.4	0.8	Hydrophobic and buried region	1.36	12	4.1
46	T	95.6	4.7			0	0.0
46	MainCh	97.7					
47	D	96.8	1.5	2 H-bonds and exposed residue		23	7.7
47	N!	95.3	3.9		1.36	213	71.7
47	L	91.4	7.3			1	0.3
47	MainCh	97.7					
49	D	95.6	1.9	4 H-bonds and exposed residue		4	1.3
49	N!	93.7	0.4		1.36	1	0.3
49	L	93.3	4.2			2	0.7
49	MainCh	98					
55	L!	96.2	2.5	Hydrophobic and buried region	1.36	228	76.8
55	N	93.7	1.1			0	0.0
55	D	92.6	7.8			0	0.0
55	MainCh	96.9					
56	E	96.3	2.1			268	90.2
56	Q!	94.2	2.2		1.36	5	1.7
56	MainCh	97					
57	V!	97.3	2.7	Hydrophobic and buried region	1.36	135	45.6

57	T	94.6	1.4			1	0.3
57	MainCh	97.5					
60	V	85.5	0.9		1.32	1	0.3
60	I!	84.6	0.7		1.36	1	0.3
60	T	83.9	0.9			4	1.4
60	S	83	1.9			16	5.5
60	A	81.1	5.2			0	0.0
60	MainCh	96.7					
61	S	91.2	1.2	Exposed residue		21	7.1
61	K!	90	4.1		1.36	37	12.5
61	MainCh	97.6					
62	D!	97.7	1.6	4 H-bonds and exposed residue	1.82	273	91.9
62	N	96.1	6.3			22	7.4
62	L	89.8	5.5			0	0.0
62	MainCh	98.2					
65	S	87.6	1			32	10.8
65	I	86.6	0.2			16	5.4
65	K!	86.4	0.3		1.82	23	7.7
65	MainCh	97					
66	V!	98.4	1.9	Hydrophobic and buried region	1.82	191	64.3
66	T	96.5	3.6			3	1.0
66	MainCh	97.4					
67	Q	95.9	2.9			21	7.1
67	E!	93	5.7		1.82	29	9.8
67	MainCh	97.5					
69	D!	96.1	1.6	3 H-bonds and exposed residue	1.65	82	27.6
69	N	94.5	5.3			82	27.6
69	L	89.2	3.7			0	0.0
69	MainCh	96.9					
89	I!	96.6	1.7		4.59	20	6.7
89	T	94.9	0.8			11	3.7
89	V	94.1	6.4			7	2.3
	MainCh	98.4					
92	D!	98.3	2.5	Coordinating Ca2+	4.59	297	99.3
92	N	95.8	5			0	0.0
92	L	90.8	7.9			0	0.0
92	MainCh	97.8					
95	Q!	97.3	2.2		4.59	263	88.0
95	E	95.1	5.2			0	0.0
95	MainCh	97.7					
101	V!	95.9	1.3	Exposed residue	4.59	8	2.7
101	T	94.6	3.5			21	7.0
101	MainCh	96.4					
104	D	95.4	0.3	1 H-bond and exposed residue		7	2.3
104	N!	95.1	1.7		4.59	6	2.0

104	L	93.4	8			0	0.0
104	MainCh	96.6					
106	V!	95.6	2.5		4.59	20	6.7
106	T	93.1	4.3			250	83.6
106	MainCh	97.8					
110	S!	96.2	2.2		3.04	14	4.7
110	T	94	6.5			4	1.3
110	MainCh	96.4					
117	D!	97.2	0.9	3 H-bonds and exposed residue	1.19	20	6.7
117	N	96.3	3.8			12	4.0
117	L	92.5	6.9			11	3.7
117	MainCh	97.9					
119	S	89.3	0.6			8	3.5
119	K	88.7	2.5			31	13.7
119	Q	80	1.2			8	3.5
119	E!	78.8	1.4		1.19	73	32.3
119	MainCh	96.7					
120	Q!	94.1	1.7		2.37	63	21.2
120	E	92.4	0.2		1.22	6	2.0
120	MainCh	97.5					
122	V!	97	1.5	Hydrophobic and buried region	2.37	65	21.9
122	T	95.5	5.3			12	4.0
122	MainCh	97.5					
124	V!	97.1	2	Hydrophobic and buried region	2.37	194	65.5
124	T	95.1	5.2			0	0.0
124	MainCh	98.3					
125	V!	97.9	1.3	Hydrophobic and buried region	2.37	91	31.1
125	T	96.6	5.6		1.19	4	1.4
125	MainCh	98.7					
126	K	91.7	3.3		1.19	8	2.7
126	R!	88.4	0.6		2.37	8	2.7
126	MainCh	97.7					
127	D!	97.6	1	4 H-bonds and exposed residue	2.37	278	93.9
127	N	96.6	5.3			4	1.4
127	L	90.4	4.9			0	0.0
127	MainCh	97.8					
128	H!	98	2.8		2.37	252	84.8
128	F	95.2	5.9			5	1.7
128	MainCh	96.9					
131	L	92.3	0.6	2 H-bonds and exposed residue		26	8.8
131	D	91.7	0.7			11	3.7
131	N!	91	5.6		2.97	112	37.8
131	MainCh	93.7					
132	N!	96.5	1.7	3 H-bonds and exposed residue	2.97	25	8.4

132	L	94.8	0.2			9	3.0
132	D	94.6	5.7			2	0.7
132	MainCh	97.2					
135	V!	97.1	1.9	Hydrophobic and buried region	2.97	164	55.4
135	T	95.2	2.7			4	1.4
135	MainCh	98					
137	V!	97.5	1.7	Hydrophobic and buried region	2.97	59	19.9
137	T	95.8	1.8			12	4.1
137	MainCh	98					
142	E!	97	2.9		2.97	282	95.3
142	Q	94.1	6.9			13	4.4
142	MainCh	97.4					
148	N	93.4	0.5	1 H-bond and exposed residue	2.97	0	0.0
148	D!	92.9	2.5			1	0.3
148	L	90.4	5.8			0	0.0
148	MainCh	96.7					
150	H!	95.2	2.7		2.97	17	5.8
150	F	92.5	1.9			4	1.4
150	MainCh	97.4					
154	T!	96.7	2.4	1 H-bond and exposed residue	2.97	11	3.8
154	V	94.3	3.4			5	1.7
154	MainCh	96.5					
167	V!	92.9	0	Exposed residue	2.21	15	5.4
167	T	92.9	0.1			28	10.0
167	I	92.8	6.7			5	1.8
167	MainCh	97.1					
171	V	95.9	0.8			33	12.0
171	T!	95.1	6.4		2.54	14	5.1
171	MainCh	97.8					
173	V	90.1	1.6	1 H-bond and exposed residue		2	0.7
173	S	88.5	1.2		2.63	36	12.9
173	T!	87.3	3.6		0.82	0	0.0
173	MainCh	96.1					
179	T	88	4.6	Double occupancy		0	0.0
179	S	83.4	0.9			0	0.0
179	C!	82.5	5.6		2.63	276	98.6
179	MainCh	96.9					
186	T!	95.3	2.5	2 H-bonds and exposed residue	2.63	33	12.0
186	V	92.8	3.6			10	3.6
186	MainCh	97					
188	L!	95.1	1	Hydrophobic and buried region	2.63	178	65.0
188	N	94.1	0.7			0	0.0
188	D	93.4	3.2		0.82	0	0.0
188	MainCh	95.7					

189	T!	96.1	2.9	1 H-bond	2.63	21	7.7
189	I	93.2	0.4			20	7.4
189	V	92.8	2.2			1	0.4
189	MainCh	96.4					
190	S	92.7	1.4			40	14.7
190	K!	91.3	4.2		2.63	82	30.1
190	MainCh	98.3					
194	Q!	96.8	0.6		1.50	48	17.7
194	E	96.2	10.8			6	2.2
194	MainCh	97.7					
198	N!	95.1	2.8	Coordinating Ca2+	0.82	213	82.6
198	D	92.3	6.2			33	12.8
198	L	86.1	2.9			0	0.0
198	MainCh	95.9					
199	K	84.1	0.3			51	20.2
199	E!	83.8	0.9		0.82	23	9.1
199	A	82.9	4.2			26	10.3
199	L	78.7	0.3			19	7.5
199	S	78.4	0			4	1.6
199	Q	78.4	0.4			2	0.8
199	MainCh	96.1					

Res# stands for residue number; ResType for residues type; RSCC for real-space correlation coefficient; ΔCont for contrast difference within other RSCC; MainCh for main chain atoms; MS for mass spectrometry; H-bond for hydrogen bond; ! for resolved residue.

Supplementary Table 10: Residues of metalloproteinase having ambiguity assignment from both crystallographic and mass spectrometry data but being resolved by phylogenetic analysis

		Crystallography			MS	ConSurf	
Res#	ResType	RSCC	ΔCont	Observation	PrimaryScore	n	%
15	N!	96	0.2	3 H-bonds	2.99	124	46.8
15	D	95.8	2.8		3.03	3	1.1
15	L	93	7.8			0	0.0
15	MainCh	97.3					
71	N!	89.5	1.8	Density looks like	1.05	59	19.8
71	D	87.7	3	is covalently bound		42	14.1
71	K	81.4	1.8			7	2.3
71	R	77.5	0.6		1.65	7	2.3
71	MainCh	97.1					
82	E!	96.3	3		1.80	66	22.1
82	Q	93.3	3.4		1.05	48	16.1
82	MainCh	97.4					
84	N	91.9	0.8	4 H-bonds and exposed	1.15	21	8.7
84	D!	91.1	4.3		1.80	70	28.9
84	L	78.8	2			0	0.0
84	MainCh	96.5					
85	L!	96.5	5	Hydrophobic and buried	1.15	284	95.0

85	N	91.5	1			0	0.0
85	D	90.5	6.8		1.80	0	0.0
85	MainCh	97.5					
86	L!	96.7	5.3		1.80	209	70.1
86	N	91.4	1.3		1.15	1	0.3
86	D	90.1	6.3			0	0.0
86	MainCh	97.5					
146	N!	98	0.6	4 H-bonds and buried	2.26	275	92.9
146	D	97.4	4		2.97	1	0.3
146	L	93.4	0.1			0	0.0
146	MainCh	97.2					
147	L!	96.4	3.5	Hydrophobic and buried	2.97	184	62.2
147	N	92.9	0.8		2.26	0	0.0
147	D	92.1	5.2			0	0.0
147	MainCh	97.8					
152	D!	97.3	2.9	3 H-bonds and buried	2.97	288	98.0
152	N	94.4	6.1		2.26	2	0.7
152	L	88.3	4.7			0	0.0
152	MainCh	98					
153	D!	95.6	0.2	3 H-bonds and exposed	2.97	52	17.7
153	N	95.4	0.2			27	9.2
153	L	95.2	4.3		2.26	10	3.4
153	MainCh	96.2					
178	V	87.2	1.1		2.54	0	0.0
178	T!	86.1	1.9		2.63	21	7.5
178	MainCh	96.4					

Res# stands for residue number; ResType for residues type; RSCC for real-space correlation coefficient; ΔCont for contrast difference within other RSCC; MainCh for main chain atoms; MS for mass spectrometry; H-bond for hydrogen bond; ! for resolved residue.

Supplementary Table 11: Residues of metalloproteinase having ambiguity assignment from crystallographic, mass spectrometry and phylogenetic analysis data

		Crystallography			MS	ConSurf	
Res#	ResType	RSCC	ΔCont	Observation	PrimaryScore	n	%
24	N?	97.4	2	2 H-bonds	2.36	88	32.6
24	D?	95.4	4.2		2.21	120	44.4
24	L	91.2	7.3			1	0.4
24	MainCh	96.8					
26	N?	88	4.7	1 H-bond and exposed residue	2.36	35	13.3
26	L	83.3	0.7			1	0.4
26	D?	82.6	1.8		2.24	31	11.8
26	S	80.8	0.3			6	2.3
26	MainCh	96.9					
181	Q?	96.1	4.7		2.54	38	13.6
181	E?	91.4	1.2		2.63	17	6.1
181	MainCh	97.7					

182	N?	89.8	1.2	2 H-bonds and exposed residue	2.54	22	7.9
182	L	88.6	2			1	0.4
182	D?	84.2	2.8		2.63	14	5.0
182	MainCh	97.2					
183	Q?	95.8	0		2.54	52	18.6
183	E?	95.8	7.2		2.63	46	16.4
183	MainCh	97.4					
185	Q?	92	3.2		2.63	50	18.1
185	E?	88.8	1.4		2.54	68	24.5
185	MainCh	96.8					

Res# stands for residue number; ResType for residues type; RSCC for real-space correlation coefficient; ΔCont for contrast difference within other RSCC; MainCh for main chain atoms; MS for mass spectrometry; H-bond for hydrogen bond; ! for resolved residue.

Supplementary Table 12: Residues of MjTX-I resolved by crystallography and MS and/or phylogenetic analysis

		Cryst mon ABCD		Cryst mon A		Cryst mon B		Cryst mon C		Cryst mon D		MS	ConSurf	
Res#	ResType	RSCC	ΔCont	RSCC	ΔCont	RSCC	ΔCont	RSCC	ΔCont	RSCC	ΔCont	PrimaryScore	#Struct	%
1	S	90.5	10.6	91.5	6.4	94.9	4.4	93.3	11.4			3.49	40	100.0
2	L	91.1	13.1	93.6	3.8			85.2	11.7			3.49	114	78.1
3	V	86.9	9.6					87.9	4.6	79	10.2	3.49	25	14.5
5	L	92.5	5	95.2	5.4	92.9	3.6	89.7	4.1	89.6	5.5	3.49	95	47.0
6	G	85.7	21.7	94	29.4	92.4	18.8	69.4	4.9	81	32.1	3.49	62	29.4
7	K					91.6	6.0						63	29.6
8	M	95.3	5					95.4	5.7	87.8	4.6	3.49	171	79.5
9	I	93.6	3.6					94.8	4.4	91.2	7	3.49	161	74.2
10	L	90.3	7	91.7	3.1	92	4.4			84.2	5.1	3.49	11	5.0
11	Q	91.8	3.6							88.5	9.3	3.49	24	11.0
12	E	94.4	3.4					93.2	5.1	93.8	5.9	3.49	9	4.0
13	T	94.8	5.5	96.7	5.6	93.8	6	95	5.7	94.2	5.7	3.49	176	72.7
14	G	86.5	31.3	89.7	21.5	90.8	28.8	78	18	83.3	34.8	3.49	198	77.6
15	K					88	4.1			88.4	3.8	3.49	102	36.8
16	N	89.5	5.2	91.6	4.3			91	5.5	88.5	5.3	2.45	72	25.6
17	P	91.8	14	92.4	12.8	95.9	19.9	92.1	11.7	87.4	1.1	3.84	141	49.3
20	S	91	10.1	86.8	3.5	92.6	10.3	91.2	5.1	94.4	8.6	3.84	75	25.3
21	Y	95.6	8.7	96.1	9.3	95.8	7.3	94.8	5.4	96	10.7	3.84	248	83.5
22	G	77.4	25.4	81.3	24.9	86.9	24.3	70.5	11.2	51.2	3	3.84	41	13.9
23	A	89.8	10.7	91.4	17.3	93.7	8.4	83.6	12.9	87.5	23.1	3.84	13	4.4
24	Y	95.9	6	95.6	6.8	95.6	5.2	96.1	5.4	95.4	4.3	3.84	297	99.7
25	G	85.3	10.7	92.6	18.1	91.6	11.3	83.9	14.4	77.5	21.1	3.84	297	99.7
26	C	96.7	14.6	97.6	16	97.4	11.3	95.4	15.5	95.9	15.7	3.84	295	98.7
27	N	95.8	13.5	97.3	11.4	95.6	9.4	94.2	12.9	95.6	13.3	3.73	10	3.3
28	C	96.5	7	96.9	6.4	96.2	5.7	95.7	8.1	96.7	6	3.84	300	100.0
29	G	82.5	23	87	28.4	87.8	11.4	73.4	16.3	74.9	23.3	3.84	294	98.0
30	V	92.6	4.8					93.5	4.2	85.8	4.4	3.84	17	5.7
31	L	86.5	4.6			93.6	3.7			79.3	4.7	3.84	5	1.7
32	G	82.1	35.6	93	27.3	89.2	18.2	69	20.2	60.1	41.3	3.84	291	97.0
33	R	91.4	6.1	93.7	11	93	3.4	91.5	5.7			3.84	61	20.3
34	G	88.5	23.5	90.4	22.6	91.9	17.5	80.3	23.3	89	28.1	3.42	278	92.7

36	P	91.7	13.2	93.5	14.7	89.8	8.9	92.6	4.2	91.2	20.6	3.42	290	96.7
37	K	89.7	8	94.2	7.2	92.4	6.1			93.3	8.4	3.42	77	25.7
38	D							96	4.3			1.38	299	99.7
39	A	88.7	13.1	88.3	7.7	94	18.5	83.3	12	89.8	8.6	1.38	120	40.0
40	T					93.8	3.3					1.38	140	46.7
41	D									93.8	3.6	1.38	298	99.3
42	R			90.8	4.1	88.6	6.8					1.38	169	56.3
43	C	95.9	14.4	97.7	16.3	92.3	9.1	94.8	13	97.6	13.7	1.65	300	100.0
44	C	96.8	12.1	97	9.1	97	14.3	96	10	97.3	13.3	1.65	300	100.0
45	Y	92.4	8.1	94.1	4.4	92.9	10.9	89.7	4.7			1.65	12	4.0
46	V	92.6	7.8	93.4	4.8	92.2	4.1	93.6	5.3	94.3	7.3	1.65	81	27.0
47	H	95.5	3.2	97.1	3.8	95.8	3.3	94.5	3			1.65	298	99.3
48	K	95.1	14.5	94.7	13.8	94.9	11.4	96.3	15.3	94.5	11.9	1.65	7	2.3
49	C	94.7	11.8	96	11.6	94.5	9	96.3	12.6	93.6	5.8	0.86	175	58.3
50	C	95	31.9	97.2	36	96.2	14.9	94.2	20.5	92.8	10.4	0.86	300	100.0
51	Y	94.3	13.8	95.2	13.5	95.5	15.1	95.1	11.5	88.9	6.1	0.86	286	95.3
54	L	88.7	4.6			88.6	6.5			87.6	3.6	2.25	118	39.3
55	T					90.6	3.6					2.25	30	10.2
57	C	91.8	8.9	94	10.7	93.2	8.6	85.9	6.6	90.2	4.7		295	98.3
58	N	85.4	5.8					83.8	4.8	88.9	7.8	2.25	70	23.6
59	P	90.1	10.2			94.1	11.7	89.5	8.9	90.6	16.2	2.25	191	64.1
60	K									70.2[α]	4.4	2.25	127	42.5
61	K					90.9	7.1						8	2.7
62	D	92	5.6	93.9	4.4	94.1	3.9	92.3	3.3	88.6	4.1	2.42	61	20.5
63	R	83.9	3.9					90.1	3.7	81.2	4.6	2.42	36	12.1
64	Y	94.6	6.4	95.3	5.6	95.6	3.3	93.5	8.1	89.5	6.1	2.42	281	94.3
65	S	85.7	9.6			87.1	7	86.4	6.7	76.6	7.8	2.42	89	29.9
66	Y	94.3	6.8	94.4	6.4	95.5	7.4	92.6	5.3	93.8	8.4	2.42	143	48.0
67	S	84.7	3.5			93	4.4	85.6	7.2			2.42	116	39.1
68	W	94.6	13.4	95.1	10	96.4	8.9	92.6	9.7	92.6	12	2.42	17	5.7
71	K	91.4	11.1	93.3	10.4	94	9.6	89.6	5.8	92.3	8.9	2.42	38	12.9
72	T	92.4	6.1					91	3.7	90.9	7	2.51	62	21.0
73	I	92.9	6.9			93.2	6.7	93	5.3	88.9	11.6	2.51	146	49.0
74	V	89.1	4	92.6	4.9			86.8	5.9			2.51	55	18.5
75	C	93.6	17.5	98.1	16	97.4	25.4	83	2.8	93	11.7	2.51	296	99.7
76	G	75.6	19.2	85.7	28.8	80.8	11					2.51	80	26.8

79	N	86.3	4.6			89.6	4.2					1.77	65	21.8
81	C	92	14.1	93.3	13.3	94.7	13.2	93	16.7	84	9.2	2.51	292	98.0
82	L	90	4.1	92.1	3.5							2.51	12	4.1
83	K	83.5	6.1	93.4	9.1			88.9	8.6	88.3	8.4	2.51	81	27.3
85	L	91.7	4.7	95.6	4.1			90.8	5.3	88[α]	3.9	2.52	87	29.3
86	C	93.3	15.5	97.2	16.6	95.6	15.9	87.4	10	91.1	13.1	2.52	297	100.0
87	E	94	6			95.2	5.4	91.3	5.4	90.4	6.9	2.52	151	50.8
88	C	96.3	17.2	97.7	12.5	97.3	17.1	96.8	12.3	92.8	16.9	2.52	296	99.7
90	K	92.5	6.2	93.7	9.4	93.3	3.7	93.7	8.6			2.52	107	36.0
91	A	89.1	16.2	94.9	10.6	82.2	5.2	92.7	12.1	86.5	12.2	2.52	78	26.4
92	V							92.3	3.1	92.8	3.9	2.52	32	10.8
93	A	93.4	15.4	95.2	5.3	95	13	90.8	13.2	87.1	14.9	2.52	248	84.1
94	I	93.2	5	95.8	3.7			94.5	4.4	89.3	4.7	2.52	53	18.0
95	C	95.6	13.4	96.1	14.4	96.1	8.2	97	14	97.8	21	2.52	295	100.0
96	L	94	6.4	93.9	4.6	92.9	10.6	94.5	6.9	95.4	4.7	2.52	82	27.9
97	R	89.9	4.9	94.9	6.9	91.7	5.6	86.7	6.2			2.52	64	22.1
98	E			95.2	3.1	87.4	3.7					2.37	27	9.9
99	N					91.9	3.5	95.4	3.1			2.37	97	38.8
100	L			93.8	3.6			89.3	3.1			2.37	79	56.0
102	T	91.1	4.9	92.6	5.1	89.8	8.8			92.8	3.5	2.37	108	45.4
103	Y	94.9	6	96.1	6.5	93.7	3.6	95.8	6.2	94.2	4.5	2.37	216	91.1
104	N					93.6	4.2	94.8	3.9			2.37	135	57.2
105	K			93	8.8							2.37	85	36.3
106	K			88.5	8							2.85	91	39.7
107	Y	87.4	4.9	91.7	6.4					94.4	7	2.85	150	67.0
108	K			78.1	5.3							2.85	63	30.9
111	Y			85.4	4							3.09	5	4.0
114	P							73.5	8.6	76.3	7.8	3.09	17	14.4
115	F			89.1	6.8					89.4	5.6	3.09	10	8.8
117	D							87.0	3.3				3	3.9
116	C	95.3	14.1	97.1	16.6	96.4	15	94.8	12.8	95.4	16.3	3.09	109	99.1
118	K	94.8	9.4	96.1	10.2	96.3	8.7	91.3	6	95.4	9	1.3	11	20.8
119	A	80.8	7.7	81.6	10.6	85.6	4.8	69.6	4.7	89.5	9	1.3	7	15.6
122	C	89.7	16.1	94	21.9	84.7	12.3	93.8	14.9	91.2	16.9	1.3	16	94.1

Res# stands for residue number; ResType for residues type; Cryst for crystallography, mon for monomer, RSCC for real-space correlation coefficient; ΔCont for contrast difference within other RSCC; MS for mass spectrometry. RSCC numbers with $^{\alpha}$ refers to RSCC of main-chain being between 70 and 80, and $^{\beta}$ refers to values below 70.

Supplementary Table 13: Residues of MjTX-I having assignment ambiguity from crystallographic data being resolved by mass spectrometry

		Cryst mon ABCD		Cryst mon A		Cryst mon B		Cryst mon C		Cryst mon D		MS	ConSurf	
Res#	ResType	RSCC	ΔCon	RSCC	ΔCon	RSCC	ΔCon	RSCC	ΔCon	RSCC	ΔCon	PrimScore	#Struct	%
1	S!									75.9	2.4	3.49	40	100
1	MainCh									90.8				
2	L!					92.5	2.2			89.6	1.5	3.49	114	78.1
2	MainCh					95.7				90.9				
3	V!			85.1	1.5	94.4	0.1					3.49	25	14.5
3	MainCh			94.8		95.5								
4	E!	92.7	2	92.9	6.8	95.4	0.6	95.3	2	83.9	0.7	3.49	47	25
4	Q	90.7	5.6	93.2	0.3	94.8	5.3	93.3	4.5	81	0.5	1.25	90	47.9
4	MainCh	93.8		95		95.4		92.4		92				
7	S	81.9	1.3	82.1	1			81.5	4.4	76	2.9		27	12.7
7	K!	73.9	1.4	89.8	1.8			63.4*	1.2	n/a*	n/a	3.49	63	29.6
7	MainCh	92.1		92.4				89.2		89				
8	M!			96.2	2.8	97	0.1					3.49	171	79.5
8	MainCh			94.2		97.5		91.3						
9	I!			94	0.5	94.3	2.7					3.49	161	74.2
9	MainCh			95.8		94.9		93						
10	L!							83.2	2.3			3.49	11	5
10	MainCh			95.5		93.8		92.5						
11	Q!			94.3	0	92.5	2.6	89.3	1.6			3.49	24	11
11	E			94.3	4.8	88.9	3.6	87.7	3.3			1.27	10	4.6

11	MainCh			95.7		94.1		94						
12	E!			94.1	0.8	96	2.5					3.49	9	4
12	Q			93.3	3.9	93.5	3						0	0
12	MainCh			93.5		94		93.4						
15	K!	84.9	0.7	83.1	1.3			89.1	2.5			3.49	102	36.8
15	MainCh	93.5		93.6				92.8						
18	A	78	0.9	83.1	1.2	89.2	5.7	67.9	2.4	78.4	2	2.6	10	5.3
18	V!	77.1	2.9	86.1	0.1	83.5	4.2	71.6	0	76.4	3.3	3.84	29	15.4
18	T	74.2	0.6	86	1.1	76.8	3.5	71.6	0	73.1	2.2	2.19	8	4.3
18	I	72.9	0.5	81.9	4.2	73.3	3.5	74.5	2.9	70.3	0.9	2.44	35	18.6
18	MainCh	90.8		92.5		94.5		89.1		88				
19	V	80.3	0.2	77.9	0.5	87.1	1.1	85.8	0.9	77.5	3.1		11	3.8
19	T!	80.1	0.6	80.7	2.8	86	0.8	84.9	1.7	79.8	2.3	3.84	19	6.5
19	S	79.5	0.6	83.7	3	81.7	2	80.9	2.5	83.7	3.9	1.24	11	3.8
19	I	78.9	4.4	86.2	2.5	84	2.3	83.2	2.3	74.4	1.3		10	3.4
19	K	61.8	1.8	65.4	0.6	66.3	6.7	66.7	0.8	70.7	5.6	2.6	11	3.8
19	MainCh	82.7		90.9		77.1		82.3		87.2				
30	V!			95.6	1.4	91.8	6.1					3.84	17	5.7
30	T			94.2	5.9	91.9	0.1					1.51	4	1.3
30	MainCh			94.4		95.7								
31	L!			88	1.2			84.2	1.9			3.84	5	1.7
31	N			86.8	0.4			82.3	5.9				1	0.3
31	D			86.4	5.8			70.8	1			1.51	2	0.7
31	MainCh			95.7				91						
33	R!									87.3	0.8	3.84	61	20.3
33	MainCh									92.2				
35	A	83.5	2.4	91	12.5	82.6	2.1	79.9	0.4	79.6	1		4	1.3
35	S	81.1	7.6	75.3	3.3	86.9	3.8	79.5	5.8	82.6	3		15	5

35	K!	65.1	0.5	76.7	1.4	83.1	0.5	73.7	1.2	n/a	n/a	3.42	28	9.3
35	MainCh	92.2		94.5		90.8		94.7		90.4				
37	K!							81.6	0.6			3.42	77	25.7
37	MainCh							86.6						
38	D!	95.6	2.2	96.4	1.4	95	1.7			97.3	1.4	1.38	299	99.7
38	N	93.4	11.4	95	9.4	93.3	7.4			95.9	9.1		0	0
38	L	82	1.3	85.6	2.1	81.5	0.4			86.8	6.6		0	0
38	MainCh	95.2		94.4		97.3				97.9				
40	T!	94.7	2.8	95.9	2.8			93.7	2.7	94.5	0.7	1.38	140	46.7
40	V	91.9	6.5	93.1	7.8			91	5.1	93.8	9.5		26	8.7
40	MainCh	94.2		95.6				93.8		93.7				
41	D!	94.8	1.1	96.3	0.5	94.8	1.1	93.9	2.9			1.38	298	99.3
41	N	93.7	3.7	95.8	4	93.7	1.5	91	3				0	0
41	L	90	0.1	91.8	0.2	92.2	2.2	88	0.6				0	0
41	MainCh	93.9		96.3		94.3		92.2						
42	R!	86.2	2.7					88	1.5	84.4	0.9	1.38	169	56.3
42	MainCh	94						91.8		95.2				
45	Y!									91.1	2.6	1.65	12	4
45	MainCh									93				
47	H!									94	2.9	1.65	298	99.3
47	MainCh									91.9				
53	T	74.6	0.6	71.1	2.2	83.3	2.7	67.2	0.3	79.6	1.2		5	1.7
53	K!	74	0.8	79.8	3	76.1	1.5	76.7	1.1	76.5	1.1	2.25	79	26.3
53	V	73.2	0.2	68.9	0.4	80.6	1.5	64.7	1.2	82	2.4		4	1.3
53	A	73	1.5	82.4	2.6	74.6	1.3	69.4	0.1	73.5	6	0.86	19	6.3
53	MainCh	86.7		91.6		86.7		85.1		84.7				
54	L!			88.6	0.9			87.6	2.2			2.25	118	39.3

54	N			89	0.4			83.5	0.3				0	0
54	D			87.7	5.9			83.2	1.2				0	0
54	MainCh			93.6				89.5						
55	V	79.9	1.3	87.1	1.1			81.3	0.1	66.4	0.7		7	2.4
55	T!	78.6	0.4	88.6	1.5			78.7	12.3	58.5	0.7	2.25	30	10.2
55	S	78.2	2.2	86	4.6			81.7	0.4	64.7	0.1		14	4.7
55	I	73.5	5.3	79.1	0.3			64.3	0.1	72.6	5		10	3.4
55	MainCh	86.4		90.5				70.7		86.7				
56	D!	69.8	0.4	83.6	0.3	76.2	0.7	54*	3.5	73.2	3.6	2.25	27	9.2
56	N	69.4	0.5	86.4	2.8	87.2	8	54.5	0.5	80.7	7.5		11	3.7
56	L	68.9	6.7	83.3	6.8	79.2	0.7	47.3	0.1	69	2.4		0	0
56	MainCh	85.5		92.6		91.8		72.8		77.1				
58	N!			92	0.2	92	0.2					2.25	70	23.6
58	L			90	8.3	90	8.3						22	7.4
58	D			91.8	1.8	91.8	1.8					1.29	31	10.4
58	MainCh			93.5		92.1								
59	P!			88.1	2.5							2.25	191	64.1
59	MainCh			89.1										
60	K!	68.7	0.2	87	2.7	76.8	4	n/a*	n/a			2.25	127	42.5
60	A	68.5	0.9	81.5	2.6	80.9	4.1	61.9	9.9				1	0.3
60	G	67.6	3.9	69.2	1.8	71.6	0.3	67.5	5.6				0	0
60	MainCh	86.7		87.8		93.1		85.1		76.5				
63	R!			81.1	0.1	87.9	1.1					2.42	36	12.1
63	K			78.6	2.7	88.7	0.4						17	5.7
63	MainCh			89.9		94.7								
65	S!			88.7	2.4							2.42	89	29.9
65	MainCh			95.9										
67	S!			87	1.6					82*	5.1	2.42	116	39.1

67	A			87	0					85.8	3.8		5	1.7
67	MainCh			90.3						78.7				
69	A	75.4	3.1	84.5	0.5	81.4	3.8	80.9	1.9	56.8	1.2		9	3.1
69	S	72.3	3.6	84	4.9	82.7	0	74.3	0.6	58.9	0.4		79	27
69	L	68.7	2.5	78.3	2.7	82.7	1.3	79	3.5	50.8	0	0.98	7	2.4
69	K!	62.5	2.1	75.6*	3.3	70.1*	3.1	68.5*	2.6	53.7*	0.4	2.42	22	7.5
69	MainCh	92.2		93.8		94.3		92.6		87.4				
70	N!	84.4	5.8	86.7	0.6	92.5	0.8	77.4	0.2	74	0.4		96	32.5
70	L	78.6	0.3	85.1	4.1	89.7	0.8	74.2	3.2	62.2	0.1		0	0
70	D	78.3	1.8	86.1	1	91.7	1.9	71	1.7	60.9	0.1	2.42	44	14.9
70	MainCh	92.8		95.9		96.2		88		85.5				
72	T!			94.2	2.7	93.6	2.5					2.51	62	21
72	V			91.5	2.8	91.1	5.4						15	5.1
72	MainCh			94.9		95.5								
73	I!			92.3	1.8							2.51	146	49
73	MainCh			95.8										
74	V!					93.8	2.2			78.5	8.2	2.51	55	18.5
74	T					91.6	4.8			79.5	1	1.27	107	35.9
74	MainCh					94.5				78.4				
76	G!							78.8	2.8	53.8	1.6	2.51	80	26.8
76	MainCh							87.8		86.2				
80	S	61.1	3.8	67.5	2.3	68.9	0.6	55.6	2.6	75.5	7.2		27	9.1
80	A!	57.3	0.7	68.1	0.6	67.6	0.4	n/a	n/a	65.1	1	2.51	25	8.4
80	MainCh	81.8		88		74.2		80		86				
82	L!					95.2	2.3	91.9	1.9	78.2	0.9	2.51	12	4.1
82	S					89.2	2.6	90	3.3	79.1	0.9		4	1.4
82	N					92.9	0.6	86.7	0.7	77.3	0.1	1.77	0	0
82	D					92.3	3.1	86	1.6	76.1	1.4	2.14	16	5.4

82	MainCh					94		88.1		76.5				
83	K!					68.1*	0					2.51	81	27.3
83	A	77.4	2.6	78.9	0.5	80.6	0.3	75.9	3.2	75.2	0.8		42	14.1
83	MainCh	90.8		94.8		91.4		89.7		81.3				
84	E!	67.7	1.9	87.4	1.5	75.8	0.4	53.2*	4.1	77	0.3	2.52	24	8.1
84	Q	65.7	3.2	89.5	2.1	75.4	3.2	56.4	0.9	83.3	5.9	1.49	75	25.3
84	MainCh	90.4		94.8		89.9		88.4		85.8				
85	L!					95.4	2.5					2.52	87	29.3
85	D					92.9	0.4						0	0
85	N					92.5	8.2						2	0.7
85	MainCh					95.8								
87	E!			96.8	2.3							2.52	151	50.8
87	Q			94.5	3.2								18	6.1
87	MainCh			96.9										
89	D!	93.7	2.6	94.8	0.8	95.4	2.1	94	1.8	87.5	1.9	2.52	294	99
89	N	91.1	6.8	94	2.3	93.3	4.3	92.2	9.8	85.6	3.3		1	0.3
89	L	84.3	3.1	87.6	3.8	83.9	1.7	82.4	1.6	82.3	2.5		0	0
89	MainCh	93.4		92.8		94.8		94.5		91.1				
90	K!									92.3	1.9	2.52	107	36
90	MainCh									92.1				
92	V!	93.4	2.1	95.3	2	93.5	5.3					2.52	32	10.8
92	T	91.3	11.1	93.3	7.7	94.4	0.9						1	0.3
92	MainCh	93.7		93.9		93.9								
94	I!					92.9	1.2					2.52	53	18
94	MainCh					93.3								
97	R!									90	0.3	2.52	64	22.1
97	MainCh									94.3				

98	E!	91.4	2.8					87.2	0.4	92.8	2.1	2.37	27	9.9
98	Q	88.6	2.9					86.3	3.5	93	0.2	2.01	23	8.4
98	MainCh	93.1						90		95.3				
99	N!	93.3	2.7	94.5	2.4					93	0.1	2.37	97	38.8
99	D	90.6	0.2	91	4.1					92.9	1.9	2.01	0	0
99	L	90.4	5.6	92.1	1.1					94.1	1.1		0	0
99	MainCh	95.2		96.7						95.1				
100	L!	90.8	2.1			88.2	0.9			93.6	0.3	2.37	79	56
100	N	88.7	0.6			87.1	4.5			93.3	0.3	1.75	4	2.8
100	D	88.1	4			87.3	0.2			93	7.7		2	1.4
100	MainCh	92.1				93.2				91.8				
101	S	74.8	1.5	75.7	0.9	67.4	2.2	79.8	0.3	83.8	3.4		8	5.7
101	N	73.3	0.6	84.1	0.5	79	1.6	67.9	1	79	0.8	1.95	14	9.9
101	D!	72.7	0.9	83.6	6.2	76.1	1.3	66.9	1.1	77.9	0.8	2.37	27	19.1
101	MainCh	79.6		84.4		74		75.7		89.4				
102	T!							94.2	2.6			2.37	108	45.4
102	S							91.6	4.1				42	17.6
102	V							87.5	0.2				2	0.8
102	MainCh							89.9						
104	N!	90.9	2.7	87.8	0.3					90.7	2.6	2.37	135	57.2
104	D	88.2	1.3	87.5	3.5					88.1	0.8	2.32	22	9.3
104	L	86.9	4.1	84	0.9					87.3	3		1	0.4
104	MainCh	94.1		90						96.7				
105	S	75	2.9			77.1	1.2	69.2	1.8	68.3	2.4	1.22	13	5.6
105	A	72.1	2.3			69	0	75	5.8	71.5	0.6	1.21	1	0.4
105	K!	69.8	0.2			70.2	0.7	65.2*	1.6	73.2	1.7	2.37	85	36.3
105	MainCh	90.4				91.8		80.1		93.9				
106	S	80.1	4			78.4	8.9	80.9	1.1	86.5	3.3		18	7.9

106	K!	68.1	0.4			64.7*	0.1	70.1*	0.8	72.3*	2.5	2.85	91	39.7
106	MainCh	90.8				91.6		90.7		89.9				
107	Y!					87.2	2.2	77.4	0.6			2.85	150	67
107	K					87.6	0.4	87.1	1.8				1	0.4
107	R					89.1	1.5	87.9	0.8				0	0
107	MainCh					90.3		83.5		90.8				
108	K!	72.5	2.7			76.5	0.4	57.9	1.3	81.3	0.9	2.85	63	30.9
108	A	69.8	0.1			79.9	1.7	62.1	0.6	75.4	0.1		9	4.4
108	MainCh	83.3				89.7		72.4		91.3				
110	L	71	4.3	76	0.3	68.6	1.7	70.3	4.6	65.3	1.4	2.16	22	16.2
110	D	66.7	2.6	80.8	4.8	66.9	1.6	65.7	4.3	51.8	1.3		0	0
110	N!	59.7	0.9	86	5.2	69.1	0.5	n/a	n/a	50.2	0.5	3.09	3	2.2
110	G	58.8	0.7	58.9	0.6	70.7	1	74	3.7	75.6	10.3	1.3	0	0
110	MainCh	69.4		73		62.9		68.7		68.2				
111	F	62.1	0.5			n/a	n/a	62.5	0.3	71.6	0.3		14	11.1
111	Y!	61.6	0.4			n/a	n/a	59.7	1.6	69.9	2	3.09	5	4
111	H	61.2	0.4			n/a	n/a	61.1	0.1	74.2	1.6		2	1.6
111	A	52.2				n/a	n/a	63.3	0.2	62.5	2.3		1	0.8
111	MainCh	59.6				60.2		75		42.7				
112	G	67.8	0.5	74	2.2	n/a	n/a	n/a	n/a	n/a	n/a	1.3	1	3
112	A	67.3	0.8	67.9	0.2	68	2	74.3	1.1	68.3	2.2		0	0
112	S	65.7	1	53.9	1.4	66	0.8	77	2.7	78.7	2.7	2.15	7	21.2
112	L!	63.5	0.9	59.4*	0.5	65.2	0.5	73.2*	3.3	73.9*	1.5	3.09	2	6.1
112	N	62	0.4	51.8	1.5	69.7	0.7	68.8	1.9	72.2	3.9		1	3
112	D	61.6	6.8	50.3	2.2	69	1	66.9	1	76	2.1		0	0
112	MainCh	67.7		71.2		56.2		82.4		57				
113	L	63.6	2.5	49.2	0.5	n/a	n/a	64.5	0.6	n/a	n/a		1	0.8
113	A	61.1	1.1	n/a	n/a	n/a	n/a	68.7	4.2	n/a	n/a	1.3	5	4.2
113	K!	n/a	n/a	48.7*	0.9	n/a*	n/a	n/a*	n/a	65.4		3.09	38	31.9
113	MainCh	82.4		85.3		77.7		92.1		85.1				

114	P!	70	0.6	68.7	1.1	81.5	1.1					3.09	17	14.4
114	V	69.4	3.1	67.6	2.1	83.1	0.5						8	6.8
114	MainCh	87.3		91		92.7								
115	F!	77	1.9			83	0.7	78.2	4.5			3.09	10	8.8
115	MainCh	91.3				93.4		92.3						
117	D!	82.8	2.9	82.3	1.9	85.2	1.4			87.1	1.3		3	3.9
117	MainCh	92.7		93.4		91.6				95.2				
120	L!	78.7	1.8	83.2	1.3	82.5	1.5	79.5	0.6	81	0.8	1.3	3	8.6
120	S	76.9	0.4	81.9	1	79.1	4	76.3	2.9	80.2	1.3		2	5.7
120	N	76.5	1	80.9	0.9	81	0.9	79.7	0.2	77.7	1		2	5.7
120	D	75.5	5.2	80	1.7	80.1	1	78.9	2.4	76.7	1		3	8.6
120	MainCh	81.5		79.3		80.6		82.4		90.1				
121	P!	72	1	81	2.7	78.4	0.5	67.8*	5.1	71.2	2.7	1.3	23	79.3
121	G	71	5.6	67.8	1.1	77.1	0.1	70.6	2.8	80.7	9.5		0	0
121	MainCh	82.6		88.9		83.1		86.4		87.5				

Res# stands for residue number; ResType for residues type; Cryst for crystallography, mon for monomer, RSCC for real-space correlation coefficient; ΔCon for contrast difference within other RSCC; MS for mass spectrometry; ! for resolved residue. Residues in bold are the side chain with hydrogen bond with neighbour atom(s). Residues with * had their side chain atoms omitted due to absence of electron density. Residues in bold are the side chain with hydrogen bond with neighbour atom(s).

Supplementary Table 14: Residues of MjTX-I having ambiguity assignment from both crystallographic and mass spectrometry data but being resolved by phylogenetic analysis

		Cryst mon ABCD		Cryst mon A		Cryst mon B		Cryst mon C		Cryst mon D		MS	ConSurf	
Res#	ResType	RSCC	ΔCon	RSCC	ΔCon	RSCC	ΔCon	RSCC	ΔCon	RSCC	ΔCon	PrimScore	n	%
16	N!					91.4	1.2					2.45	72	25.6
16	D					88.1	0.2					2.6	16	5.7
16	MainCh					96								
52	G	77.8	1.3	82.4	0.3	77.2	0.7	72.9	2.9	74.3	1.3		66	22.1
52	S	76.5	0.8	84.5	2.1	76.4	1.2	76.9	1.2	71.5	1.1		35	11.7

52	K!	73.7	0.8	86.5	2	76.5	0.1	68.8	0.8	73*	0.3		28	9.4
52	I	72.8	0.9	75.1	4.3	78.2	1	79.8	2.9	70.2	2.3	0.86	2	0.7
52	MainCh	87.9		94.5		89.7		83.8		89				
61	A	70	1.4	87.6	7.3			n/a	n/a	74.5	5.2		4	1.3
61	G	68.6	0.2	67.9	2.8			n/a	n/a	77.1	2.6		0	0.0
61	S	68.4	2	80.3	0.7			67.7	0.3	59.1	0.6		13	4.3
61	K!	66.4	2.6	79,6*	0.6			n/a*	n/a	67,3*	3.7		8	2.7
61	MainCh	91.5		89.8				83.9		92.1				
70	N!	84.4	5.8	86.7	0.6	92.5	0.8	77.4	0.2	74	0.4		96	32.5
70	L	78.6	0.3	85.1	4.1	89.7	0.8	74.2	3.2	62.2	0.1		0	0.0
70	D	78.3	1.8	86.1	1	91.7	1.9	71	1.7	60.9	0.1	2.42	44	14.9
70	MainCh	92.8		95.9		96.2		88		85.5				
77	Q	61.2	2.3	79.6	1.1	65.7	0.1	59	1.2	63.5	2.7	2.14	3	1.0
77	E!	58.9	1.1	80.4	0.8	64.8	0.9	60.1	1.1	60,8*	0.5	2.51	24	8.0
77	MainCh	81.7		93.3		73		56		84.7				
78	D	75.2	1.1	91.4	0	74	1.2	65.5	1	83.1	0.2	1.27	20	6.7
78	N!	74.1	0	91.4	2.3	72.8	0.5	64.3	0	82.9	1.1	1.74	90	30.2
78	L	74.1	2.8	89.1	5.8	75.1	0.4	63.2	1.6	81.8	2.1	1.29	4	1.3
78	E	71.3	0.2	81.1	1.2	78.2	1.7	67.9	1.8	76.2	1.2	2.51	26	8.7
78	Q	66.6	0.3	67	0.4	76.5	1.4	69.7	1.1	75	1.3	2.14	29	9.7
78	MainCh	79		85.3		73.5		72		79.8				
79	N!			84.3	0.7			83.2	2.3	82.4	2.4	1.77	65	21.8
79	D			83.6	2.8			80.9	2.1	78.7	0.4	2.51	81	27.2
79	L			80.8	2.9			78.8	1.2	80	1.3		1	0.3
79	MainCh			78.6				79.6		79.8				
109	D	67.0	4.7	80.5	1.2	71.0	1.3	n/a	n/a	77.2	0.2	2.85	11	7.1
109	L	58.9	3.1	82.6	0.9	68.6	3.7	n/a	n/a	77.0	0.7		3	1.9
109	N!	50.2	0.4	81.7	1.2	73.5	1.2	n/a*	n/a	76.3	4.2	3.09	45	29.2
109	MainCh	71.1		66.4		74.2		62.7		84.4				

Res# stands for residue number; ResType for residues type; Cryst for crystallography, mon for monomer, RSCC for real-space correlation coefficient; ΔCon for contrast difference within other RSCC; MS for mass spectrometry; PrimScore for Primary Score ! for resolved residue. Residues with * had their side chain atoms omitted due to absence of electron density.

Supplementary Table 15: Residues of crotoxin resolved by crystallography and MS and/or phylogenetic analysis

Crystallography monomer A					Crystallography monomer B					MS	ConSurf	
Res#	ResType	RSCC	ΔCont	RSCC*	Res#	ResType	RSCC	ΔCont	RSCC*	PrimaryScore	n	%
					1	H	97.1	4.5	97	3.52	0	0.0
2	L	93.6	4	96.9	2	L	91.4	5.9	95.2	3.52	123	89.8
5	F	96.1	4.2	96.5	5	F	95.3	6	96.7	3.52	127	65.5
8	M	97.4	5.8	95	8	M	97.3	4.7	96.4	3.52	167	82.7
9	I	95.5	6.3	95.2	9	I	96.1	3.5	96	3.52	175	85.4
10	K	91	9	96.8	10	K	92	6.8	95.3	3.52	83	40.3
					11	F	96.1	6.1	95.1	3.52	4	1.9
13	T	94.8	5.8	94.1	13	T	96.8	3.6	96	3.52	144	68.6
14	R	88.5	6.4	91	14	R	84.9	3.7	94.9	3.52	12	5.6
15	K	84.9	8.6	93.6	15	K	90.2	4	96.3	6.32	89	40.1
16	N	88.1	3.9	94.4						6.32	59	26.3
17	A	92.5	11.9	92	17	A	92.1	21	93.3	6.32	98	43.0
19	P	96.3	16.1	97	19	P	96.1	16	97	6.32	10	4.2
20	F	96	4.5	96.9	20	F	95	4.3	96.8	6.32	6	2.3
21	Y	95.8	6	96.4	21	Y	96.4	6.6	95.2	6.32	236	81.1
22	A	83.8	11.3	92.1	22	A	88.4	14	92.9	6.32	43	14.7
23	F	94	5.3	95.5	23	F	95.9	2.7	84.3	6.32	37	12.4
24	Y	97.1	7.8	96	24	Y	95.2	6	95.4	6.32	296	99.3
25	G	93.2	17.4	95.9	25	G	90.5	19	95.3	6.32	297	99.7
26	C	95.7	16.8	94.2	26	C	94.5	13	94.4	6.32	294	98.7
27	Y	94.1	5.3	95	27	Y	95.6	7.7	95.9	6.32	225	75.5
28	C	97.2	18.1	94.9	28	C	95.6	10	86.2	6.32	297	99.7
29	G	61.8	4.6	89.9	29	G	37.9	4.7	79.1	6.32	289	97.0
30	W	95	8.4	96.4	30	W	81	3.9	83.4	6.32	43	14.4
31	G	90.5	31.7	95.1	31	G	64.7	30	83.1	6.32	261	87.6
32	G	87.6	13.3	95.3	32	G	81.3	17	90.4	6.32	281	94.3
33	Q	91.4	6.5	94.5	33	A	78	4.8	92.5	6.32 / -	41 / 8	13.8 / 2.7

34	G	88.3	16.7	94.7	34	G	91	17	96.6	6.32	275	92.3
36	P	89	14.8	89.6	36	P	94.5	10	95	4.95	290	97.3
37	A	89.6	13.4	91.7	37	K	90.9	4.5	93.2	- / 4.95	3 / 72	1.0 / 24,2
39	A	91.8	21.1	95.7	39	A	94.4	25	95.6	3.27	97	32.6
					41	D	96.9	3.2	95.2	3.27	298	99.7
					42	R	87	8.6	94.2	3.55	163	54.3
43	C	95.6	7.6	95.7	43	C	95	8.5	94	3.55	297	99.7
44	C	95.7	16.8	96.5	44	C	95.2	8	94.4	3.55	298	100.0
45	F	94.3	4.2	95.4	45	F	95.2	3.4	93	3.55	60	20.1
46	V	92.6	6.2	95	46	V	92.4	4.6	96.5	3.55	80	26.8
47	H	94	5	93.8	47	H	96.7	3.9	95.5	3.55	294	98.3
48	D	87.6	3.8	95.5						3.55	261	87.3
49	C	95.5	14.2	94.8	49	C	95.7	11	95	3.55	169	56.5
50	C	94.3	10.7	94.1	50	C	95.1	7.5	96.2	3.55	298	99.7
51	Y	93.5	6	93.5	51	Y	96.7	6.7	95.5	3.55	281	94.0
52	G	82.3	34.1	93.1	52	G	82.7	23	92	3.55	79	26.4
53	K	90.6	5.7	91.5	53	K	91.1	6.6	92.7	3.55	81	27.1
54	L	92.2	4.7	92.6	54	L	92.6	5.6	95.1	1.39	109	36.5
56	K	91	6.7	90.4	56	K	87.6	9.3	93	1.39	14	4.8
57	C	92.7	13.6	90	57	C	96.8	16	97.2	3.94	294	98.7
					60	N	89.9	4.9	95		2	0.7
61	W	93.1	7.7	87.1	61	W	95.7	9.7	95	3.94	15	5.0
62	N	72.4	3.8	84.4	62	N	95.3	3.9	96.7		26	8.7
64	Y	94.9	4.4	95.4	64	Y	95.2	5.9	94.1	3.94	277	92.3
65	R	75.9	4.4	86.1	65	R	90	4.7	95.1	2.77	23	7.7
66	Y	93.1	6.7	83.5	66	Y	96.5	3.6	94.5	3.94	142	47.5
67	S	86.2	6.4	92.2	67	S	89.8	3.6	95	3.94	104	34.8
68	L	93.2	5.9	93.5	68	L	93.4	3.9	95	3.94	8	2.7
					69	A	77.5	7	88.5		19	6.3
					70	S	95.8	13	94.8	3.00	25	8.3
71	G	87	35.1	91.7	71	G	86.4	23	94.1	3.00	113	37.7
72	Y	93.6	7.6	90.6	72	Y	93.5	3.7	93.4	3.00	3	1.0
					73	I	95.5	5.8	95.7	3.00	143	47.7
74	T	84.3	3.9	88.5						3.00	113	37.7
75	C	92	10.3	89.3	75	C	95.8	18	95.3	3.00	298	99.7
76	G	69	None	87.8	76	G	88.5	32	94.5	3.00	53	17.9

77	G	73.5	13.4	87.8	77	K	82.5	7	91.9	- / 3.00	40 / 42	13.7 / 14.3
78	G	65.8	8.7	75.6	78	G	83	14	94.3	3.97	52	17.9
					79	T	92.5	4.3	93.8	3.97	52	17.9
80	W	92.4	9.7	93.2	80	W	96.5	12	95.1	3.97	26	8.9
81	C	91.4	8.1	91.2	81	C	93.6	8.4	94.5	3.97	280	96.2
82	E	85.8	7.4	94.2						3.97	90	31.0
83	E	88.3	3.1	95.2						3.97	11	3.8
84	Q	89	5.2	96.7	84	Q	95.4	3.9	96.6	3.97	59	20.3
86	C	93.5	3.2	93.8	86	C	96.6	15	94.2	3.97	289	100.0
					87	E	93	4.8	95.6	3.97	126	43.9
88	C	96.3	8.5	95.6	88	C	96.6	14	96.7	3.97	287	99.3
90	R	95	6.5	95.7	90	R	94.3	3.6	96	3.97	124	43.1
					91	V	95.2	4	97	3.80	24	8.4
92	A	95.8	17.9	97.7	92	A	93.8	11	96.9	3.80	199	69.3
93	A	93.3	14.1	95.8	93	A	95.1	20	97	3.80	236	82.2
94	E	93	6.4	95.8	94	E	90.2	2.6	93.6	3.80	52	18.1
					95	C	94	14	95.9	3.80	284	99.0
96	L	95.6	3	94.3	96	L	96.4	3.2	97.8	3.80	83	28.9
97	R	92.5	3.8	95.5	97	R	92.5	3.8	95.9	3.80	53	18.7
98	A	86.3	5.3	91.3	98	R	95.4	5.5	94.6	3.64 / 2.99	24 / 70	9.5 / 27,8
99	S	94	11	95.4	99	S	96.2	11	96.4	3.74	35	15.0
101	S	82.8	8.7	90.6	101	S	81.5	4.8		3.74	7	6.0
102	T	94.1	3.9	93.9	102	T	94.4	5	95.1	3.74	89	41.2
103	Y	95.3	5.7	90.1	103	Y	94.7	4.6	95.6	3.74	172	83.5
104	T	89.1	6	92.9						3.64	3	1.5
105	N	91	4.2	90.8	105	Y	93.2	1.9	96.7	3.74 / 2.99	22 / 0	11.1 / 0,0
106	G	72.5	7	90.4	106	G	92.6	25	94.2	3.74	4	2.1
107	Y	91.2	3.1	94	107	Y	94.9	3	96.1	3.74	119	61.7
108	M	95.4	6	95.6	108	M	95	0.8	92.6	3.74	9	4.8
109	F	96.4	3.2	94.3	109	F	96.2	3.5	90.6	3.74	46	24.7
110	Y	96.4	4.8	94.8	110	Y	95	3	96.1	3.74	92	51.1
111	P	83	12.4	90	111	P	91.5	16	92.2	3.74	104	58.4
					112	D	88.1	6.4	93.7	3.74	32	18.1
113	S	77.9	8	83.2						3.74	23	12.8
114	R	84.4	3.6	88.6	114	R	83	1.4	93	3.74	33	18.5
115	C	96	18.2	83.3	115	C	89.1	7	88.6	1.25	179	100.0

116	G	57.7	5.2	65.7	116	G	53.9	None	73.1	1.25	41	27.5
118	A	84.4	11.4	80.9	118	P	92	18	91.2	- / 1.25	4 / 35	3.0 / 26,1
119	S	86.8	8.6	90.5						1.25	23	18.7
122	C	85.4	12.4	77.2	122	C	61.1	7.9	76.7	1.25	108	100.0

Res# stands for residue number; ResType for residues type; RSCC for real-space correlation coefficient; ΔCont for contrast difference within other RSCC; *for main chain atoms; MS for mass spectrometry.

Supplementary Table 16: Residues of crotoxin having assignment ambiguity from crystallographic data being resolved by mass spectrometry

Crystallography monomer A					MS	ConSurf		Crystallography monomer B						ConSurf	
Res#	ResType	RSCC	ΔCo	Observation	PrScore	n	%	Res#	ResType	RSCC	ΔCo	Observation	PrScore	n	%
1	S!	73.2	0.5		3.09										
1	K	72.7	0.1												
1	T	72.6	1.3												
1	V	71.3	1.5												
1	MainCh	90.1													
3	V	74.2	1.3			20	12.2	3	L!	93	0.2		3.52	79	48.2
3	L!	72.9	0.7		3.52	79	48.2	3	N	92.9	1.4			0	0.0
3	A	72.2	2			4	2.4	3	D	91.4	6.2			0	0.0
3	MainCh	90.6						3	MainCh	94.8					
4	E	93.2	2.1			30	16.0	4	Q!	96.8	2		3.52	109	58.3
4	Q!	91.2	5		3.52	109	58.3	4	E	94.8	8.9			30	16.0
4	MainCh	95						4	MainCh	97.1					
6	D	88.8	3.5			3	1.5	6	N!	94.5	0.5	3 H-bonds	3.52	16	8.2
6	N!	85.3	3.8		3.52	16	8.2	6	D	94	5.8			3	1.5
6	L	81.5	0.6			0	0.0	6	MainCh	96.8					
7	T	89.3	5.6			11	5.6	7	V	87.8	1.6			6	3.0
7	V	83.7	3.9			6	3.0	7	T	86.2	1.5			11	5.6
7	S	79.8	1.3			37	18.7	7	S	84.7	1.6			37	18.7
7	K!	62.1	0.5		3.52	38	19.2	7	K!	83.1	0.4		3.52	38	19.2
7	MainCh	94.3						7	MainCh	95.9					
11	F!	94.5	2.8		3.52	4	1.9								

11	H	91.7	3.1		19	9.2								
11	MainCh	94.7												
12	E!	93.9	1.8	3.52	12	5.8	12	E!	94.7	1		3.52	12	5.8
12	Q	92.2	5.4		0	0.0	12	Q	93.7	5.4			0	0.0
12	MainCh	92.6					12	MainCh	96.3					
							16	N!	93.8	1.7		6.32	59	26.3
							16	L	92.1	2.1			3	1.3
							16	S	90.0	2.8			68	30.4
							16	D	87.2	6.5			10	4.5
							16	MainCh	95.8					
18	V!	90.9	0.4	6.32	23	13.6	18	I!	92.2	2.4		5.47	27	16.0
18	T	90.5	3.9		6	3.6	18	V	89.8	2.2		6.32	23	13.6
18	MainCh	95.2					18	T	87.6	2.3			6	3.6
							18	MainCh	95.9					
35	A	77.9	1.7		5	1.7	35	R!	86.2	1.8		6.32	21	7.0
35	R!*	67.3	2.1	6.32	21	7.0	35	K	84.4	4.9			14	4.7
35	MainCh	95.7							95.7					
38	D!	95.2	1.2	3.27	297	99.7	38	D!	97	2.2		3.27	297	99.7
38	N	94	8.3		0	0.0	38	N	94.8	6.4			0	0.0
38	MainCh	94.7					38	MainCh	95					
40	T!	94.8	1.5	3.27	126	42.3	40	T!	95.7	1.8	1 H-bond	3.27	126	42.3
40	V	93.3	8		29	9.7	40	V	93.9	4.9			29	9.7
40	MainCh	96.3					40	MainCh	96.2					
42	R!	84	0.3	3.55	163	54.3								
42	A	92			4	1.3								
42	MainCh	95.1												
							48	D!	89.5	1		3.55	261	87.3
							48	S	88.5	3.5			0	0.0

								48	MainCh	94.3					
55	A!	70.2	0.8		1.39	14	4.7	55	G	79.2	0.7			7	2.3
55	G	69.5	8.6			7	2.3	55	A!	78.5	27		1.39	14	4.7
55	MainCh	86.6						55	MainCh	94.4					
58	N!	81.4	2.9	1 H-bond	3.94	41	13.8	58	N!	96.4	2.5	2 H-bonds	3.94	41	13.8
58	D	78.5	4.8			21	7.0	58	D	93.9	3.8			21	7.0
58	MainCh	80.2						58	MainCh	96.3					
59	V	88	0.7	1 H-bond		8	2.7	59	T!	95.8	1.9	1 H-bond	3.94	36	12.1
59	T!	87.3	3.1		3.94	36	12.1	59	V	93.9	5.6			8	2.7
59	MainCh	86.7						59	MainCh	95.9					
63	V	89.1	1.6			12	4.0	63	T	91.7	0.1			32	10.7
63	T	87.5	3.1			32	10.7	63	V	91.6	1.4			12	4.0
63	I!	84.4	2.7		3.94	20	6.7	63	I!	90.2	5.1		3.94	20	6.7
63	MainCh	90.4						63	MainCh	97.2					
70	S!	83.5	0.8		3.00	25	8.3								
70	G	82.7	1.2			44	14.7								
70	A	81.5	11.2			8	2.7								
70	MainCh	87													
73	I!	93.7	2.7		3.00	143	47.7								
73	T	91.0	0.2			7	2.3								
73	V	90.8	7.6			74	24.7								
73	MainCh	87.6													
79	T!	82.9	1.4		3.97	52	17.9								
79	S	81.5	5.6			55	18.9								
79	MainCh	86.7													
								83	E!	94.3	1.4		3.97	11	3.8
								83	Q	92.9	5.9			21	7.2
								83	MainCh	91.8					

85	I!	94.3	2.3		3.97	77	26.6	85	I!	92.5	0.1		3.97	77	26.6
85	T	91.9	0.7			23	7.9	85	V	92.4	2			54	18.6
85	V	91.2	5.3			54	18.6	85	T	90.4	1.5			23	7.9
85	MainCh	96.5						85	MainCh	96.4					
87	E!	93.7	2.1		3.97	126	43.9	87	E!	93	4.8		3.97	126	43.9
87	Q	91.6	7.7			20	7.0	87	MainCh	95.6					
87	MainCh	96.3													
89	D!	96.9	1.5	4 H-bonds	3.97	283	97.9	89	D!	96.9	1.7	4 H-bonds	3.97	283	97.9
89	N	95.4	3.6			2	0.7	89	N	95.2	7			2	0.7
89	MainCh	96.2						89	MainCh	97.9					
91	V!	95.3	1.3		3.97	24	8.4								
91	T	94	2.8			42	14.6								
91	MainCh	96.5													
95	C!	91.3	0.2		3.97	284	99.0								
95	S	91.1	27.0			1	0.3								
95	MainCh	93.6													
								104	L	84.1	0.8		3.74	0	0.0
								104	A	83.2	0.7			0	0.0
								104	S	82.6	5.5			13	6.5
								104	K!	77	1.4		2.99	13	6.5
								104	N	75.7	1.3			106	52.7
								104	D	74.4	4.1			12	6.0
								104	MainCh	95.1					
112	K	68.7	1.8			16	9.0								
112	R	66.8	0.8			26	14.7								
112	M	66.1	0.1			0	0.0								
112	A	65.9	0.3			3	1.7								
112	D!	49.1	4.4		3.74	32	18.1								
112	MainCh	86.2													

117	G!		1.25	72	50.0	117	G!	57.4		1.25	72	50.0
117	MainCh	60.3				117	MainCh	74.7				

Res# stands for residue number; ResType for residues type; RSCC for real-space correlation coefficient; ΔCo for contrast difference within other RSCC; MainCh for main chain atoms; MS for mass spectrometry; H-bond for hydrogen bond; ! for resolved residue.

Supplementary Table 17: Residues of crotoxin having ambiguity assignment from both crystallographic and mass spectrometry data but being resolved by phylogenetic analysis

Crystallography monomer A				MS	ConSurf		Crystallography monomer B				MS	ConSurf	
Res#	ResType	RSCC	ΔCont	PrimaryScore	n	%	Res#	ResType	RSCC	ΔCont	PrimaryScore	n	%
60	N!	83	2.4		2	0.7							
60	L	81.1	0.5		6	2.0							
60	MainCh	88											
69	A!	68	0.1		19	6.3							
69	N	68	0.9		9	3.0							
69	D	67	2.1		7	2.3							
69	MainCh	75											
							74	T!	94.1	0.8	3.00	113	37.7
							74	V	93.3	7.6		46	15.3
							74	MainCh	95.6				
82	E!	82	2	3.97	90	31.0	82	E!	93.3	0.6	3.97	90	31.0
82	Q	80	1.3	3.80	63	21.7	82	Q	92.6	4.1	3.80	63	21.7
82	MainCh	95											
100	D	95	1	3.74	0	0.0	100	D	95.6	1.2	3.74	0	0.0
100	L!	94	0.8	2.99	55	47.4	100	L!	94.4	0.3	2.99	55	47.4
100	N	93	5.5	3.64	0	0.0	100	N	94	8.8	3.64	0	0.0
100	MainCh	95					100	MainCh	95.7				
120	E!	93	2.3	1.25	19	16.4	120	E!	93.4	1.4	1.25	19	16.4
120	Q	91	4.6		1	0.9	120	Q	92	4.8		1	0.9

120	MainCh	88					120	MainCh	95.3				
121	T!	73	1.4	1.25	30	26.8	121	T!	89.6	2.9	0.38	30	26.8
121	I	71	0.3		0	0.0	121	V	86.7	7.1		0	0.0
121	V	71	2.3		0	0.0	121	MainCh	90.7	5.1			

Res# stands for residue number; ResType for residues type; RSCC for real-space correlation coefficient; ΔCont for contrast difference within other RSCC; MainCh for main chain atoms; MS for mass spectrometry; PrScore for PrimaryScore; H-bond for hydrogen bond; ! for resolved residue.