Table S1. pKa Values Calculated for Resonances with pH Dependant Chemical Shifts.

Given in this table are the pKa values calculated for pH dependant resonances in the given peptides, dominant pKas and c values are highlighted in light gray. The value c_i is the fraction of the total chemical shift displacement contributed by the ith titration event (having pKa_i). The acidic amino acids in the sequence are color matched to their corresponding pKa's in other resonances they affect. The total chemical shift change during the titration for each resonance is given in the column labeled $\Delta\delta$ (ppm). For each peptide, the activity on NPR-1 is given as a percent of the measured activity of EMPGVLRF-NH_2. Only sufficiently resolved backbone amide resonances with a total chemical shift change of greater than 0.02 ppm were included in this table. (Table on next page)

* = Chemical shift changed directions during pH titration; ** = "1" being the farthest downfield of two similar protons.

Peptide	Peak	Δδ (ppm)	pKa_1	c_1	pKa_2	c_2
DFDGAM-NH_2	D1 alpha	0.12789	3.23 ± 0.02	1	-	-
	D1 beta	0.2635	3.19 ± 0.02	1	-	-
Activity:	F2 amide	0.02219	4.04 ± 0.04	1	-	-
0%	F2 beta 1 **	-0.04182	3.82 ± 0.02	1	-	-
	D3 alpha	0.10395	4.09 ± 0.03	1	-	-
	D3 beta	0.25764	4.13 ± 0.03	1	-	-
	D3 amide	0.143935	4.11 ± 0.01	1	-	-
	G4 amide	-0.274427	4.15 ± 0.08	0.61	3.18 ± 0.14	0.39
	A5 amide	-0.08342	4.02 ± 0.02	0.70	2.81 ± 0.07	0.30
	M6 amide	0.03094	3.93 ± 0.02	1	-	-
DFDGAMPGVLRF-NH_2	D1 alpha	0.14664	2.97 ± 0.02	0.84	4.18 ± 0.10	0.16
	F2 amide	0.02355	3.80 ± 0.24	1	-	-
Activity:	D3 amide	0.14108	4.04 ±0.01	1	-	-
29.1 %	G4 amide	-0.2852	4.10 ± 0.04	0.63	3.05 ± 0.07	0.36
	A5 amide	-0.08525	3.99 ± --	0.70	2.85 ± --	0.30
	M6 amide	0.04743	4.48 ± 0.11	0.51	3.51 ± 0.10	0.49
	G8 amide	-0.03288	4.34 ± 0.07	0.61	3.02 ± 0.12	0.39
	V9 amide	0.03112	3.74 ± 0.05	0.65	4.78 ± --	0.35
	R11 epsilon	-0.01513	4.21 ± 0.10	0.54	2.84 ± 0.13	0.46
DFDGEMPGVLRF-NH_2	F2 amide	-0.0074 *	4.68 ± 0.05	0.57	3.71 ± 0.04	0.43
	D3 amide	0.14832	3.63 ± 0.05	0.52	4.55 ± 0.07	0.48
Activity:	G4 amide	-0.2028	2.97 ± 0.03	0.55	3.87 ± 0.03	0.45
19.0 %	E5 amide	-0.1611	4.59 ± 0.02	0.75	3.08 ± 0.04	0.25
	M6 amide	-0.00707 *	4.74 ± 0.03	0.57	3.09 ± 0.03	0.43
	G8 amide	-0.05852	4.51 ± 0.04	0.61	3.24 ± 0.05	0.39
	V9 amide	0.05953	3.31 ± 0.04	0.53	4.48 ± 0.05	0.47
	R11 epsilon	-0.0414	4.53 ± 0.03	0.78	3.00 ± 0.09	0.22
DFDGEMSMPGVLRF-NH_2	F2 amide	-0.01648 *	4.59 ± 0.09	0.56	4.13 ± 0.10	0.44
	D3 amide	0.14966	3.72 ± 0.05	0.54	4.62 ± 0.07	0.46
Activity:	G4 amide	-0.20381	2.99 ± 0.08	0.50	3.74 ± 0.07	0.50
45.0 %	E5 amide	-0.17421	4.65 ± 0.02	0.73	3.19 ± 0.05	0.27
	M6 amide	0.0413	3.40 ± 0.02	1	-	-
	M8 amide	0.05752	3.34 ± 0.05	0.65	4.62 ± 0.12	0.35
	G10 amide	-0.0454	4.62 ± 0.05	0.59	3.24 ± 0.05	0.41
	V11 amide	0.05247	3.43 ± 0.04	0.53	4.69 ± 0.06	0.47
	R13 epsilon	-0.0175	4.58 ± 0.04	0.73	2.88 ± 0.11	0.27

Peptide	Peak	Δδ (ppm)	pKa_1	c_1	pKa_2	c_2
GFGDEM-NH_2	F2 amide	-0.10392	**3.51 ± 0.03**	0.80	**4.43 ± 0.11**	0.20
	G3 amide	-0.12881	**3.52 ± 0.04**	0.51	**4.45 ± 0.05**	0.49
Activity:	**D4 amide**	0.29597	**3.51 ± 0.00**	1	-	-
0 %	**E5 amide**	-0.17321	**4.41 ± 0.01**	1	-	-
	M6 amide	-0.00302 *	**3.30 ± 0.05**	0.52	**4.50 ± 0.06**	0.48
	CNH_2 1 **	0.04575	**4.24 ± 0.02**	1		
GFGDEMSMPGVLRF-NH_2	F2 amide	-0.09853	**3.50 ± 0.03**	0.88	**4.34 ± 0.19**	0.12
	G3 amide	-0.12611	**3.68 ± 0.05**	0.66	**4.56 ± 0.13**	0.34
Activity:	**D4 amide**	0.29564	**3.47 ± 0.01**	1	-	-
49.3 %	**E5 amide**	-0.20448	**4.31 ± 0.01**	1	-	-
	M6 amide	0.01312 *	**4.49 ± 0.05**	0.71	**2.98 ± 0.12**	0.29
	S7 amide	0.05786	**3.75 ± 0.07**	0.75	**5.03 ± 0.44**	0.25
	M8 amide	0.05181	**3.63 ± 0.05**	0.78	**5.21 ± 0.47**	0.22
	G10 amide	-0.03699	**4.19 ± 0.07**	0.78	**2.66 ± 0.33**	0.22
	V11 amide	0.03465	**3.87 ± 0.07**	0.71	**5.24 ± 0.43**	0.29
	R13 epsilon	-0.01783	**4.07 ± 0.02**	0.83	**2.32 ± 0.24**	0.17
GFGDAMPGVLRF-NH_2	F2 amide	-0.06875	**3.46 ± 0.008**	1	-	-
	G3 amide	-0.05954	**3.47 ± 0.007**	1	-	-
Activity:	**D4 amide**	0.35	**3.50 ± 0.01**	1	-	-
104.8 %	M6 amide	-0.01985	**3.58 ± 0.06**	1	-	-
	G8 amide	-0.02524	**3.51 ± 0.01**	1	-	-
	R11 epsilon	-0.00689	**3.34 ± 0.03**	1	-	-
EMPGVLRF-NH_2	**E1 alpha**	0.0404	**3.74 ± 0.02**	1	-	-
	M2 amide	-0.0882	**3.57 ± 0.02**	1	-	-
Activity:	G4 amide	-0.0491	**3.65 ± 0.01**	1	-	-
100 %	V5 amide	0.037	**3.80 ± 0.04**	1	-	-
	R7 epsilon	-0.0283	**3.56 ± 0.02**	1	-	-

Table S2. ^{1}H NMR assignments for all peptides examined in the current study.

All assignments in this table are for spectra obtained from samples at pH 5.5.

Peptide	Amino Acid	Resonance	Chemical Shift (ppm)
DFDGAM-NH_2	Asp 1	Hα	4.179
		Hβ	2.652
		Hβ	2.759
	Phe 2	H	8.828
		Hα	4.629
		Hβ	3.079
		Hβ	3.122
	Asp 3	H	8.433
		Hα	4.543
		Hβ	2.629
	Gly 4	H	7.991
		Hα	3.876
	Ala 5	H	8.250
		Hα	4.285
		Hβ	1.401
	Met 6	H	8.331
		Hα	4.416
		Hβ/ε	2.025
			2.110
		Hγ	2.519
		Hγ	2.628
	C-NH_2	a	7.510
		b	7.198
DFDGAMPGVLRF-NH_2	Asp 1	Hα	4.179
		Hβ	2.737
	Phe 2	H	8.824
		Hα	4.629
		Hβ	3.079
		Hβ	3.123
	Asp 3	H	8.442
		Hα	4.542
		Hβ	2.627
	Gly 4	H	7.912
		Hα	3.854
	Ala 5	H	8.130
		Hα	4.286
		Hβ	1.358
	Met 6	H	8.351
		Hα	4.758
		Hβ/ε	1.940
			2.048
		Hγ	2.543
		Hγ	2.630
	Pro 7	Hα	4.394
	Gly 8	H	8.582
		Hα	3.919
	Val 9	H	7.899
		Hα	4.070
		Hβ	2.068
		Hγ	0.906

Peptide	Amino Acid	Resonance	Chemical Shift (ppm)
DFDGAMPGVLRF-NH_2 Continued	Leu 10	H	8.375
		Hα	4.306
		Hβ/γ	1.486
			1.611
		Hδ	0.862
		Hδ	0.927
	Arg 11	H	8.281
		Hα	4.242
		Hβ	1.444
		Hβ	1.659
		Hγ	1.659
		Hδ	3.102
		Hε	7.168
	Phe 12	H	8.267
		Hα	4.609
		Hβ	2.994
		Hβ	3.165
	C-NH_2	a	7.593
		b	7.149
DFDGEMPGVLRF-NH_2	Asp 1	Hα	4.180
		Hβ	2.652
		Hβ	2.738
	Phe 2	H	8.799
		Hα	4.630
		Hβ	3.079
		Hβ	3.123
	Asp 3	H	8.468
		Hα	4.543
		Hβ	2.628
	Gly 4	H	7.890
		Hα	3.876
	Glu 5	H	8.209
		Hα	4.263
		Hβ	1.874
		Hβ	2.014
		Hγ	2.218
		Hγ	2.260
	Met 6	H	8.516
		Hα	4.759
		Hβ/ε	1.952
			2.048
		Hγ	2.541
		Hγ	2.606
	Pro 7	Hα	4.395
	Gly 8	H	8.614
		Hα	3.900
		Hα	3.943
	Val 9	H	7.876
		Hα	4.070
		Hβ	2.068

Peptide	Amino Acid	Resonance	Chemical Shift (ppm)
DFDGEMPGVLRF-NH_2 Continued		Hγ	0.905
	Leu 10	H	8.358
		Hα	4.328
		Hβ/γ	1.487
			1.617
		Hδ	0.862
		Hδ	0.927
	Arg 11	H	8.296
		Hα	4.241
		Hβ/γ	1.402
			1.465
			1.659
		Hδ	3.101
		Hε	7.195
	Phe 12	H	8.274
		Hα	4.608
		Hβ	2.993
		Hβ	3.166
	C-NH_2	a	7.581
		b	7.148
DFDGEMSMPGVLRF-NH_2	Asp 1	Hα	4.180
		Hβ	2.662
		Hβ	2.759
	Phe 2	H	8.801
		Hα	4.611
		Hβ	3.082
		Hβ	3.125
	Asp 3	H	8.470
		Hα	4.546
		Hβ	2.631
	Gly 4	H	7.980
		Hα	3.901
	Glu 5	H	8.284
		Hα	4.244
		Hβ	1.919
		Hβ	2.047
		Hγ	2.286
	Met 6	H	8.438
		Hα	4.482
		Hβ/ε	2.006
			2.093
		Hγ	2.501
		Hγ	2.608
	Ser 7	H	8.317
		Hα	4.417
		Hb	3.835
	Met 8	H	8.335
		Hα	4.803
		Hβ/ε	1.942

Peptide	Amino Acid	Resonance	Chemical Shift (ppm)
DFDGEMSMPGVLRF-NH_2 Continued		Hβ/ε	2.071
		Hγ	2.545
		Hγ	2.609
	Pro 9	Hα	4.395
		Hβ	1.921
		Hβ	2.071
	Gly 10	H	8.610
		Hα	3.879
		Hα	3.965
	Val 11	H	7.883
		Hα	4.073
		Hβ	2.071
		Hγ	0.909
	Leu 12	H	8.374
		Hα	4.331
		Hβ/γ	1.488
			1.619
			1.619
		Hδ	0.866
		Hδ	0.930
	Arg 13	H	8.295
		Hα	4.243
		Hβ/γ	1.402
			1.468
			1.662
		Hδ	3.103
		Hε	7.173
	Phe 14	H	8.282
		Hα	4.611
		Hβ	2.995
		Hβ	3.168
	C-NH_2	a	7.585
		b	7.149
GFGDEM-NH_2	Gly 1	Hα	3.769
		Hα	3.810
	Phe 2	H	8.803
		Hα	4.542
		Hβ	3.078
	Gly 3	H	8.698
		Hα	3.722
		Hα	3.961
	Asp 4	H	8.049
		Hα	4.585
		Hβ	2.690
	Glu 5	H	8.658
		Hα	4.240
		Hβ	1.977
		Hβ	2.068
		Hγ	2.303
	Met 6	H	8.408

Peptide	Amino Acid	Resonance	Chemical Shift (ppm)
GFGDEM-NH_2 Continued		Hα	4.433
		Hβ/ε	2.022
			2.109
		Hγ	2.496
		Hγ	2.615
	CNH_2	a	7.565
		b	7.184
GFGDEMSMPGVLRF-NH_2	Gly 1	Hα	3.765
		Hα	3.809
	Phe 2	H	8.801
		Hα	4.562
		Hβ	3.055
		Hβ	3.120
	Gly 3	H	8.695
		Hα	3.746
		Hα	3.959
	Asp 4	H	8.047
		Hα	4.584
		Hβ	2.690
	Glu 5	H	8.662
		Hα	4.240
		Hβ	1.958
		Hβ	2.065
		Hγ	2.298
	Met 6	H	8.387
		Hα	4.477
		Hβ/ε	2.025
			2.090
		Hγ	2.507
		Hγ	2.604
	Ser 7	H	8.263
		Hα	4.433
		Hb	3.852
	Met 8	H	8.325
		Hα	4.799
		Hβ/ε	1.958
			2.066
		Hγ	2.539
		Hγ	2.626
	Pro 9	Hα	4.390
		Hβ	1.917
		Hβ	2.065
	Gly 10	H	8.606
		Hα	3.894
		Hα	3.960
	Val 11	H	7.897
		Hα	4.067
		Hβ	2.066
		Hγ	0.903
	Leu 12	H	8.373
		Hα	4.326

Peptide	Amino Acid	Resonance	Chemical Shift (ppm)
GFGDEMSMPGVLRF-NH_2 Continued		Hβ/γ	1.485
			1.614
		Hδ	0.861
		Hδ	0.926
	Arg 13	H	8.290
		Hα	4.239
		Hβ/γ	1.416
			1.463
			1.656
		Hδ	3.098
		Hε	7.172
	Phe 14	H	8.279
		Hα	4.606
		Hβ	2.990
		Hβ	3.164
	C-NH_2	a	7.588
		b	7.149
GFGDAMPGVLRF-NH_2	Gly 1	Hα	3.833
	Phe 2	H	8.797
		Hα	4.541
		Hβ	3.078
	Gly 3	H	8.623
		Hα	3.723
		Hα	3.916
	Asp 4	H	7.936
		Hα	4.541
		Hβ	2.647
	Ala 5	H	8.354
		Hα	4.283
		Hβ	1.356
	Met 6	H	8.405
		Hα	4.756
		Hβ/ε	1.937
			2.066
		Hγ	2.539
		Hγ	2.625
	Pro 7	Hα	4.402
		Hβ	1.938
		Hβ	2.068
	Gly 8	H	8.573
		Hα	3.918
	Val 9	H	7.931
		Hα	4.067
		Hβ	2.065
		Hγ	0.904
	Leu 10	H	8.378
		Hα	4.325
		Hβ/γ	1.482
			1.614
		Hδ	0.861
		Hδ	0.925

Peptide	Amino Acid	Resonance	Chemical Shift (ppm)
GFGDAMPGVLRF-NH_2 Continued	Arg 11	H	8.289
		Hα	4.240
		Hβ/γ	1.356
			1.420
			1.657
		Hδ	3.119
		Hε	7.167
	Phe 12	H	8.273
		Hα	4.606
		Hβ	2.991
		Hβ	3.164
	C-NH_2	a	7.600
		b	7.147
EMPGVLRF-NH_2	Glu 1	H	4.046
	Met 2	H	8.997
		Hα	4.843
		Hβ/ε	1.980
			2.110
		Hγ	2.605
		Hγ	2.669
	Pro 3	Hα	4.434
	Gly 4	H	8.576
		Hα	3.938
	Val 5	H	7.918
		Hα	4.068
		Hβ	2.066
		Hγ	0.925
	Leu 6	H	8.354
		Hα	4.326
		Hβ/γ	1.486
			1.614
		Hδ	0.861
		Hδ	0.926
	Arg 7	H	8.281
		Hα	4.240
		Hβ/γ	1.421
			1.485
			1.657
		Hδ	3.120
		Hε	7.178
	Phe 8	H	8.261
		Hα	4.607
		Hβ	2.992
		Hβ	3.186
	C-NH_2	a	7.587
		b	7.135
SGSGAMPGVLRF-NH_2	Gly 2	H	8.824
		Hα	4.091
	Ser 3	H	8.552
		Hα	4.479
		Hβ	3.933

Peptide	Amino Acid	Resonance	Chemical Shift (ppm)
SGSGAMPGVLRF-NH_2 Continued	Gly 4	H	8.560
		Hα	3.941
	Ala 5	H	8.208
		Hα	4.306
		Hβ	1.336
	Met 6	H	8.482
		Hα	4.780
		Hβ/ε	1.961
			2.068
		Hγ	2.563
		Hγ	2.649
	Pro 7	Hα	4.414
	Gly 8	H	8.560
		Hα	3.941
	Val 9	H	7.966
		Hα	4.070
		Hβ	2.068
		Hγ	0.905
	Leu 10	H	8.391
		Hα	4.328
		Hβ/γ	1.486
			1.595
		Hδ	0.863
		Hδ	0.927
	Arg 11	H	8.297
		Hα	4.241
		Hβ/γ	1.463
			1.658
		Hδ	3.122
		Hε	7.166
	Phe 12	H	8.281
		Hα	4.608
		Hβ	2.995
		Hβ	3.166
	C-NH_2	a	7.607
		b	7.150
AAAAAMPGVLRF-NH_2	Ala 1	Hα	4.073
	Ala 2	H	8.659
		Hα	4.317
		Hβ	1.379
	Ala 3	H	8.518
		Hα	4.263
		Hβ	1.379
	Ala 4	H	8.395
		Hα	4.262
		Hβ	1.368
	Ala 5	H	8.359
		Hα	4.286
		Hβ	1.357
	Met 6	H	8.443
		Hα	4.780

Peptide	Amino Acid	Resonance	Chemical Shift (ppm)
AAAAAMPGVLRF-NH_2 Continued		Hβ/ε	1.939
			2.068
		Hγ	2.563
		Hγ	2.650
	Pro 7	Hα	4.418
		Hβ	1.943
		Hβ	2.072
	Gly 8	H	8.554
		Hα	3.940
	Val 9	H	7.964
		Hα	4.070
		Hβ	2.068
		Hγ	0.904
	Leu 10	H	8.386
		Hα	4.328
		Hβ/γ	1.486
			1.617
		Hδ	0.862
		Hδ	0.928
	Arg 11	H	8.298
		Hα	4.242
		Hβ/γ	1.422
			1.659
		Hδ	3.122
		Hε	7.168
	Phe 12	H	8.282
		Hα	4.608
		Hβ	2.994
		Hβ	3.165
	C-NH_2	a	7.604
		b	7.147
PGVLRF-NH_2	Pro 1	H	9.090
		H	8.410
		Hα	4.436
		Hβ/γ	2.456
			2.069
		Hδ	3.404
	Gly 2	H	8.745
		Hα	3.995
		Hα	4.050
	Val 3	H	8.291
		Hα	4.092
		Hβ	2.025
		Hγ	0.906
	Leu 4	H	8.447
		Hα	4.329
		Hβ/γ	1.466
			1.595
		Hδ	0.863
		Hδ	0.928
	Arg 5	H	8.371

Peptide	Amino Acid	Resonance	Chemical Shift (ppm)
PGVLRF-NH_2 Continued		Hα	4.264
		Hβ/γ	1.442
			1.509
			1.661
		Hδ	3.123
		Hε	7.167
	Phe 6	H	8.318
		Hα	4.608
		Hβ	2.994
		Hβ	3.166
	C-NH_2	a	7.632
		b	7.136
PGVLRFPGVLRF-NH_2	Pro 1	H	9.090
		H	8.413
		Hα	4.434
		Hβ/γ	2.066
			2.453
		Hδ	3.410
	Gly 2	H	8.746
		Hα	3.982
		Hα	4.046
	Val 3	H	8.287
		Hα	4.079
		Hβ	2.014
		Hγ	0.903
	Leu 4	H	8.438
		Hα	4.326
		Hβ/γ	1.442
			1.570
		Hδ	0.839
		Hδ	0.925
	Arg 5	H	8.327
		Hα	4.240
		Hβ/γ	1.420
			1.507
			1.636
		Hδ	3.119
		Hε	7.205
	Phe 6	H	8.403
		Hα	4.326
		Hβ	2.927
		Hβ	3.142
	Pro 7	H1α	3.767
		H2α	3.595
	Gly 8	H1	8.610
		H1α	3.874
		H2	8.115
		H2α	3.938
	Val 9	H1	8.094
		H2	8.054
		H1α	4.068

Peptide	Amino Acid	Resonance	Chemical Shift (ppm)
PGVLRFPGVLRF-NH_2		H1α	4.068
Continued		H2α	4.088
		H1β	2.023
		H2β	2.068
		H1γ	0.882
		H2γ	0.925
	Leu 10	H	8.403
		Hα	4.326
		Hβ/γ	1.464
			1.605
		Hδ	0.839
		Hδ	0.904
	Arg 11	H	8.300
		Hα	4.239
		Hβ/γ	1.420
			1.466
			1.657
		Hδ	3.111
		Hε	7.169
	Phe 12	H	8.279
		Hα	4.606
		Hβ	2.991
		Hβ	3.164
	C-NH_2	a	7.614
		b	7.154