## Supplementary Information for

## Structured cyclic peptides that bind the EH domain of EHD1

Alissa J. Kamens,<sup>a</sup> Robyn J. Eisert,<sup>a</sup> Tiffany Corlin,<sup>b</sup> James Baleja,<sup>b</sup> and Joshua A. Kritzer<sup>a</sup>

<sup>a</sup> Department of Chemistry, Tufts University, 62 Talbot Ave., Medford, MA 02155

<sup>b</sup> Department of Developmental, Molecular, and Chemical Biology, Tufts University School of Medicine, 136 Harrison Ave., Boston, MA 02111.

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**Protein preparation.** The EH domains were prepared from plasmids encoding the EH domain of EHD1 (EHD1-EH) and the second EH domain of Eps15 (Eps15-EH2), as described.<sup>[1]</sup> The EH domains were expressed in BL21 cells as a glutathione S-transferase (GST) fusion and were purified on a glutathione-agarose column (Gold Biotechnology).<sup>[1,2]</sup> The EH domains were cleaved from the glutathione-agarose column with thrombin (Sigma Aldrich), and thrombin was removed via a benzamidine-agarose column (Sigma Aldrich). Proteins were dialyzed in buffer (25 mM MOPS, 1 mM CaCl<sub>2</sub>, pH = 7.0) using 3.5 KDa MWCO dialyzers (Thermo-Scientific) at 4°C.<sup>[1]</sup> The purity of each protein was verified by SDS-PAGE with a 4-20% SDS gradient gel (Bio-Rad), and all proteins were determined to be >95 % pure (Figure S1A, B). Concentrations were measured by absorbance at 280 nm, using an extinction coefficient of 13980 M<sup>-1</sup>cm<sup>-1</sup>.



Figure S1. (a) SDS-PAGE of samples from EHD1-EH preparation. (b) SDS-PAGE of samples from Eps15-EH2 preparation. The contents of each lane are listed above the image. Serial dilutions (1:5, 1:25, and 1:125) are shown to verify protein purity.

**Peptide synthesis and purification.** Materials were purchased from EMD Biosciences, Anaspec and Creosalis. All peptides were synthesized by solid-phase peptide synthesis (SPPS), using standard 9-fluoromethyloxycarbonyl (Fmoc) chemistry. Unless otherwise indicated, all fluoresceinated peptides were labeled on resin by coupling 5(6)-carboxyfluorescein succinimidyl ester. All of the peptides were purified by reverse-phase HPLC (Varian Prostar) on a C18 preparatory scale column and H<sub>2</sub>O/CH<sub>3</sub>CN with 0.1% trifluoroacetic acid, using a 5-55 % CH<sub>3</sub>CN:H<sub>2</sub>O gradient over 30 minutes. The peptides were then re-purified on a C18 analytical scale column as needed, until the final product was  $\geq 95\%$  pure. The lyophilized peptides were dissolved in dimethyl sulfoxide to prepare final stock solutions. Concentrations were determined in by absorbance at 274 nm with an extinction coefficient of 1280 M<sup>-1</sup>cm<sup>-1</sup> in the assay buffer described below. The concentrations of fluorescently labeled peptides were determined with an extinction coefficient of 77,700  $M^{-1}$  cm<sup>-1</sup> in 50 mM Tris (pH = 9.0), 150 mM NaCl, and 2.5 mM CaCl<sub>2</sub>. Retention times are listed for a C18 analytical column and guard column. The peptides' identities were confirmed via ESI (Thermoscientific Finnigan LTQ) or MALDI-TOF (Bruker Microflex) mass spectrometry. Pure peptides were stored as concentrated stocks in dimethylsulfoxide (DMSO).

Table S1. Peptide preparation data. Masses detected by MALDI-TOF unless otherwise noted.									
Peptide	Sequence	Retention	Expected	Observed					
		time	Mass	Mass					
		(min)	(m/z)	(m/z)					
Linear	Ac-YNPFEEGG-CONH <sub>2</sub>	17.0	952.4	953.4 <sup>a</sup>					
cNPF1	-YNPFEEGG-	18.0	893.4	894.4 <sup>a</sup>					
Linear-Flu	(Flu)- $\beta\beta$ YNPFEE-CONH <sub>2</sub>	21.8	1296.5	1297.5 <sup>a</sup>					
cNPF1-Flu	-YNPFEEGK(Flu)-	23.5	1322.5	1321.2					
cNPF2-Flu	-YNPFEEγK(Flu)-	23.2	1349.5	1348.1					
cNPF3-Flu	-YNPFEEK(Flu)-	23.1	1265.5	1263.3					
cNPF4-Flu	-YNPFEAGK(Flu)-	23.8	1264.5	1262.6					
cNPF5-Flu	-YNPFAEGK(Flu)-	23.9	1264.5	1262.9					
cNPF6-Flu	-YNPFEQGK(Flu)-	23.0	1321.5	1320.4					
cAPA-Flu	-YAPAEEGK(Flu)-	20.1	1203.5	1204.5 <sup>a</sup>					
cNPF1B	-YNPFEEGK(Ac)-	18.8	1006.4	1004.9					
cNPF5	-YNPFAEGK-	19.7 <sup>b</sup>	835.4	834.1					
cAPA	-YAPAEEGG-	12.3	774.3	775.4 <sup>a</sup>					

<sup>a</sup> Mass taken by ESI

<sup>b</sup> On analytical C8 column

Figure S2. Chemical structures of cNPF1 (top) and the linear NPF peptide (bottom). The NPF motif is shown in red. Structures are shown in their protonation states at pH = 7.0.





**Isothermal titration calorimetry.** The experiments were performed on a Microcal ITC200 system (GE Healthcare). All proteins and peptides were dialyzed together in 25 mM MOPS, 1 mM CaCl<sub>2</sub>, and NaCl (as specified) at a pH of 7.0 at 4°C prior to the experiments. Dialyzers had a molecular weight cut-off of 3,500 Da (Thermoscientific Slide-a-lyzer, 0.5-3 mL) for protein dialysis and a molecular weight cut-off of 100-500 Da (Spectrum Labs, Micro Float-a-lyzer dialysis device) for peptide dialysis. ITC experiments were performed at 20°C with stock solutions of 20-50  $\mu$ M protein and tenfold concentration of peptide. The buffer was verified to be pH=6.8 at the experimental temperature.

Table S2. Binding data from ITC.										
Peptide	NaCl (mM)	$K_{d}(\mu M)$	ΔH°	$\Delta S^{\circ}$	Ν	Figure				
_			(kcal/mol)	(cal/mol°)		_				
Linear	0	5.24	-10.1	-10.2	0.959	S3a				
		5.65	-9.68	-9.02	1.06	S3b				
		5.99	-9.95	-10.0	1.09	S3c				
	Average	$5.6 \pm 0.6$	$-9.9 \pm 0.2$	$-9.7 \pm 0.3$	$1.04\pm0.07$	N/A				
	15	11.06	-10.1	-11.9	1.08	S3d				
		9.17	-9.33	-8.77	1.13	S3e				
		8.62	-9.06	-7.73	1.06	S3f				
		8.54	-9.07	-7.75	1.04	S3g				
	Average	$9.4 \pm 1.2$	$-9.3 \pm 0.5$	$-9.0 \pm 2.0$	$1.08\pm0.04$	N/A				
	150	33.90	-10.6	-15.5	0.951	S3h				
		40.00	-12.5	-22.4	0.872	S3i				
		33.33	-11.9	-14.3	1.07	S3j				
	Average	$35.7 \pm 3.7$	$-11.1 \pm 1.2$	$-17.4 \pm 4.9$	$0.96\pm0.06$	N/A				
cNPF1	0	1.33	-11.8	-13.3	1.03	S3k				
		1.50	-11.7	-13.1	1.04	S31				
		1.51	-11.9	-14.5	1.05	S3m				
	Average	$1.6 \pm 0.3$	$-11.8 \pm 1.3$	$-13.6 \pm 0.8$	$1.04\pm0.01$	N/A				
	15	1.84	-10.6	-9.79	1.17	S3n				
		2.61	-12.7	-17.8	0.881	S30				
		2.87	-11.5	-13.9	1.04	S3p				
		2.76	-11.9	-15.2	1.01	S3q				
	Average	$2.5 \pm 0.5$	$-11.7 \pm 0.9$	$-14.2 \pm 3.3$	$1.03 \pm 0.12$	N/A				
	150	9.62	-12.0	-17.8	1.04	S3r				
		10.74	-11.9	-17.7	1.04	S3s				
		9.23	-11.8	-17.1	1.10	S3t				
	Average	$9.9 \pm 0.8$	$-11.9 \pm 0.1$	$-17.5 \pm 0.4$	$1.06 \pm 0.03$	N/A				

The fourfold improvement in binding affinity for cNPF1 over the linear control suggested that the cyclization of NPF promoted a conformation compatible with target binding. The low affinity of the interaction between the linear peptide and EHD1 at 150 mM salt resulted in a poorer signal-to-noise ratio and larger experimental error. As a result, it was difficult to directly compare the thermodynamic parameters of the linear and cyclic peptides binding to EHD1 at physiological salt. However, the overall trends in the  $\Delta$ H and  $\Delta$ S values remained consistent as 15 mM and 0 mM salt, and suggested that the improvement in binding affinity upon cyclization was primarily enthalpic in nature. This supports the hypothesis that the cyclized NPF motif can make more favorable noncovalent interactions with EHD1-EH. Interestingly, the binding entropy ( $\Delta$ S) was more thermodynamically favorable for the linear peptide than for cNPF1 at lower salt concentrations. We have previously attributed entropy changes in EH domain binding to differences in water organization around charged residues near the NPF-binding pocket.<sup>[1]</sup> The small entropic penalty observed for cNPF1 has been seen in other cyclic molecules; evidently, the preorganization of a binding epitope does not always confer entropically favored protein-ligand interactions, and that the entropy of these interactions may be dominated by water organization rather than peptide structure.<sup>[3,4,5]</sup> The difference in  $\Delta$ S between linear and cyclic peptides was no longer observed under physiological salt conditions, perhaps because the greater concentration of NaCl lessened the organization of water around the negatively charged side-chains of the ligand and the positively charged side-chains of the protein.







Figure S3. Raw data from ITC experiments. (a-c) ITC data from experiments with the linear control with no NaCl. (d-g) ITC data from experiments with the linear control at 15 mM NaCl. (h-j) ITC data from experiments with the linear control at 150 mM NaCl. (k-m) ITC data from experiments with cNPF1 and no NaCl. (n-q) ITC data from cNPF1 experiments at 15 mM NaCl. (r-t) ITC data from experiments with cNPF1 at 150 mM NaCl.

**Fluorescence polarization (FP) assays.** All FP experiments were performed in flat-bottom, black 384 well plates (Corning). The assay buffer (25 mM MOPS, and 1 mM CaCl<sub>2</sub> at a pH of 7.0 at 4°C) had a final NaCl concentration of either 15 or 150 mM as needed. Each experiment also had a final concentration of 1.5% DMSO and 0.1% Tween-20, which were added along with the probe. The buffer was verified to be pH=6.8 at 20°C. Each probe was incubated at a final concentration of 100 nM at room temperature with varying concentrations of EHD1-EH or Eps15-EH2. The plates were spun at 1,600 G at 20°C after the addition of the probe. Fluorescence polarization was measured 1 hour after the addition of the probe, and again at 4 hours after addition of the probe (Tecan F200 Pro). No difference in the data was detected between 1 and 4 hours, and 1-hour data was used for curve fitting. K<sub>d</sub> curve fits were derived from first principles, and calculated using non-linear regression (Kaleidagraph, Synergy Software, Equation 1). The data obtained from the 150 mM NaCl experiments were fit by assuming the upper bounds observed for each probe at 15 mM NaCl. Three or more independent trials were performed on each probe, under both sets of salt conditions.

(1)  $P = P_F + (P_B - P_F) \times \frac{L_T + K_d + R_T - \sqrt{[(L_T + K_d + R_T)^2 - 4L_T R_T]}}{2}$   $P = \text{experimental polarization value, } P_F = \text{polarization of free ligand, } P_B = \text{polarization of bound ligand, } L_T = \text{total ligand concentration, } K_d = \text{dissociation constant, } R_T = \text{total concentration of protein.}$ 

Table S3. Data from FP binding assays. K <sub>d</sub> values were obtained									
from the curve fits shown in Figures 1 and S4.									
Pantida	$K_{d}(\mu M)$	$K_{d}(\mu M)$							
repude	15 mM NaCl	150 mM NaCl							
Lin-Flu	$6.9 \pm 0.6$	$31.4 \pm 0.5$							
cNPF1-Flu	$3.3 \pm 0.3$	$16.8 \pm 0.1$							
cNPF2-Flu	$4.5 \pm 0.3$	$20.5 \pm 0.3$							
cNPF3-Flu	$11.3 \pm 1.0$	$57.8 \pm 0.2$							
cNPF4-Flu	$17.4 \pm 0.1$	$46.7\pm0.9$							
cNPF5-Flu	$8.7 \pm 0.9$	$28.3\pm0.3$							
cNPF6-Flu	$12.8 \pm 0.8$	$34.0 \pm 0.3$							
cAPA-Flu	> 67	Not determined							



Figure S4. FP direct binding data. Identical data to Figure 1a are reproduced here, separated into two plots that compare different macrocycle sizes (a) and different substitutions for the negatively charged side chains (b). Data from similar direct binding assays at 150 mM NaCl are shown in (c), with curve fits shown. Curves for the data in (c) were fitted using the upper polarization limits from the data in (a) and (b) in order to extract K<sub>d</sub> values solely for comparison among the different peptides at physiological salt. (d) Direct binding experiments with Eps15-EH2. Eps15 experiments were performed with 1mM DL-dithiothreitol (Sigma Aldrich). Error bars show standard deviation from three to four independent trials. Binding experiments with Eps15-EH2 (d) were done in duplicate.

**Circular dichroism.** EHD1-EH and Eps15-EH2 was dialyzed at 4°C in 10 mM sodium phosphate buffer at pH = 7.0 with 1 mM CaCl<sub>2</sub> and 1 mM dithiothreitol. CD was performed at room temperature (Jasco J-715 circular dichroism spectropolarimeter) with EHD1-EH at 40.3  $\mu$ M and Eps15-EH2 at 35.5  $\mu$ M. Spectra were taken from 190 nm to 260 nm at 1nm intervals.



Figure S5. CD spectra of EHD1-EH (a) and Eps15-EH2 (b). The spectra for both proteins are consistent with predominantly alpha-helical secondary structure, as expected for EH domains. These results indicate that the proteins were properly folded, and that lack of binding affinity for Eps15-EH2 by cNPF1-flu results from genuine selectivity among EH domains.

**Fluorescence polarization competition assays.** All experiments were performed in flat-bottom, black 384 well plates (Corning). The assay buffers were prepared at 4°C with 25 mM MOPS with pH = 7.0, 1 mM CaCl<sub>2</sub>, and 15 mM NaCl. The experiments were performed at room temperature, at which MOPS was verified to have a pH of 6.8. Each experiment also had a final concentration of 1.5% DMSO and 0.1% Tween-20, which were added along with the probe. Each inhibitor was added and to EHD1-EH, spun at 1,600 G , and incubated at room temperature for 30 minutes. The fluorescent probes were then added to the mixture so that the final concentration of probe was 100 nM and the final concentration of EHD1-EH was 20  $\mu$ M. The plates were spun at 1,600 G at 20°C after the addition of the probe. No difference in the data was detected between 1 and 4 hours, and 1-hour data was used for curve fitting. The fluorescence polarization was measured at 1 hour and 4 hours after the addition of the probe. The IC<sub>50</sub> curve fits were calculated with a non-linear regression software (Kaleidagraph, Synergy Software, Equation 2). No deviation in fluorescence signal was observed up to DMSO concentrations of 10%.

(2)  $P = P_F + \frac{(P_B - P_F)}{(1+10^{[X-Log(IC_{50})]})}$ P = measured polarization,  $P_F =$  polarization of free probe,  $P_B =$  polarization of fully bound probe, X = concentration of inhibitor,  $IC_{50} =$  half-maximal inhibitory concentration.

**NMR Spectroscopy.** The NMR spectra were collected on a Bruker Avance 600 MHz spectrometer. The linear NPF peptide and cNPF1 were at concentrations of 1.2 mM and 4.9 mM, respectively, as determined by absorbance at 274 nm with an extinction coefficient of 1280  $M^{-1}$  cm<sup>-1</sup>. Both peptides were dissolved in 10 mM deuterated imidazole, 10 mM NaCl, 10 mM 4,4-dimethyl-4-silapentane-1-sulfonic acid (DSS) and 0.02% NaN<sub>3</sub> in a 10% D<sub>2</sub>O/90% H<sub>2</sub>O solution, which was adjusted to a pH between 5.6 and 5.9. A temperature series of <sup>1</sup>H 1D spectra for linear NPF and cNPF1 were collected in 5 °C increments from 5 °C to 25 °C. A total correlation spectroscopy (TOCSY) was collected with a mixing time of 40 ms and a rotating-frame nuclear Overhauser effect correlation spectroscopy (ROESY) was collected at a mixing time of 250 ms at 5 °C. Additionally, a <sup>13</sup>C heteronuclear single-quantum correlation spectroscopy (HSQC) and a nuclear Overhauser effect correlation spectrescopy (NOESY) with a mixing time of 200 ms were taken at 5 °C for cNPF1. Proton assignments were made according to standard homonuclear methods.<sup>[6]</sup> Distance restraints, dihedral restraints, hydrogen bond restraints, and both carbon and hydrogen chemical shifts were used in CNSSolve Version 1.3 for structure determination. Restraints were refined with CcpNMR Analysis Version 2.2 and structures were validated with CING through CcpNMR.

cNPF1	NH		HA		HB	HG		HD		HE	
Y1		8.46	4.4	6	3.12/2.91				7.13		6.85
N2		8.08	4.1	8	2.72/2.67			7.90/	7.13		
P3			4.4	9	2.05/1.42	1.86/1	1.76	3.81/	3.59		
F4		8.30	4.4	9	3.39/3.10				7.26		7.38
<i>E5</i>		7.66	4.6	52	2.11/1.86	2.25/2	2.23				
<i>E6</i>		8.94	4.1	6	2.03	2	2.29				
G7		8.87	4.26/3.7	8							
<i>G8</i>		8.07	3.81/3.9	96							
Linear											
NPF	NH		HA		HB	HG		HD		HE	
Y1		8.36	4.4	9	2.99/2.87				7.09		6.79
N2		8.49	4.9	92	2.82/2.62			7.76/	7.10		
P3			4.2	21	2.14/1.63	1	1.85	3.64/	3.40		
F4		8.02	4.5	59	3.23/3.02				7.28		6.79
E5		7.84	4.2	26	2.02/1.90	2	2.22				
<i>E6</i>		8.58	4.2	24	2.08/1.98	2	2.30				
G7		8.75	4.0	)1							
<i>G8</i>		8.38	3.9	91							
cNPF1	CA		CB		CG	CD		CE			
Y1	:	59.03	38.4	15							
N2			39.2	27							
P3	(	64.15	31.8	30	27.31	50	).68				
F4	:	58.01	37.9	8							
E5	:	54.75	32.2	20		36	5.06				
<i>E6</i>	:	57.80	31.7	75		35	5.92				
G7	4	45.22									
<i>G8</i>		45.26									

Table S4. <sup>1</sup>H chemical shifts for cNPF1 and linear NPF peptide, and carbon chemical shifts for cNPF1 determined from <sup>13</sup>C-HSQC.



Figure S6. Temperature dependence of amide proton line shapes. a) Temperature series of the amide region of <sup>1</sup>H spectra of the linear NPF peptide at 5°C (blue), 10°C (yellow), 15°C (red), and 20°C (black). b) Temperature series of the amide region of <sup>1</sup>H spectra of cNPF1 at 5°C (blue), 10°C (yellow), 15°C (red), and 20°C (black). The black arrows at 7.9ppm and 8.3ppm indicate the asparagine and phenylalanine amide peaks, respectively, which are broadening due to their involvement in a hydrogen bond within the NPF motif.

	linear NPF peptide	cNPF1
Experimental restraints		
Distance restraints from NOEs	64	135
Dihedral angle restraints	0	3
Hydrogen bond restraints	0	2
Total no. of experimental restraints	64	140
Rms deviations from experimental data		
Average distance restraint violation (Å)	$0.0 \pm 0.0$	$0.0 \pm 0.0$
Dihedral restraint violations $> 5^{\circ}$	$0.0 \pm 0.0$	$0.0 \pm 0.0$
Rms deviations from ideal stereochemistry		
Bonds (Å)	$0.0046 \pm 0.00058$	$0.0046 \pm 0.00011$
Angles (deg)	$0.4354 \pm 0.0247$	$0.6272 \pm 0.0094$
Impropers (deg)	$0.3822 \pm 0.0149$	$0.5149 \pm 0.0232$
Ramachandran analysis of the structures		
Residues in favored regions	72.5%	50.0%
Residues in additionally allowed regions	27.5%	50.0%
Residues in disallowed regions	0.0%	0.0%
Lennard-Jones potential energies		
Ensemble average (kcal/mol)	$27.30\pm2.9$	$43.98\pm0.8$
Coordinate precision (Å)		
Backbone	$0.816 \pm 0.3701$	$0.048 \pm 0.1085$
All heavy atoms	$1.343 \pm 0.4809$	$0.556 \pm 0.2674$

Table S5. NMR structural data and refinement statistics.

Iteriative   Resonances   Value (A)   Limit   Limit     1   residue   2   HA   residue   2   HB1   2.773   4.177   1.377     3   residue   2   HB1   2.771   4.177   1.372     4   residue   2   HB1   residue   2   HB2   2.302   4.442   1.632     5   residue   2   HD4   residue   2   HB2   2.400   4.976   0.000     7   residue   2   HD4   residue   2   HB2   2.480   4.978   0.000     8   residue   3   HB1   7.332   4.789   0.000     9   residue   3   HB1   7.332   4.789   0.000     9   residue   3   HB1   residue   3   HB2   2.774   3.560   2.379     12   residue   3   HB1   residue   3   HB2   2.577   3.									Upper	Lower
1   residue   2   HN   2.613   3.136   2.2090     2   residue   2   HA   residue   2   HB1   2.777   4.177   1.377     3   residue   2   HB2   residue   2   HB2   2.3032   4.432   1.632     6   residue   2   HB2   residue   2   HB2   2.480   4.796   0.000     7   residue   2   HD#   residue   2   HB4   2.332   4.798   0.000     9   residue   3   HB1   2.305   3.650   2.379     12   residue   3   HB1   residue   3   HB2   2.974   3.260   2.174     13   residue   3   HB2   residue   3   HB2   1.777   3.777   1.777   3.777   1.607   1.4   residue   3   HB2   residue   3   HB2   residue   3.403   2.222   1.7 <th>Restraint</th> <th>Resonances</th> <th></th> <th></th> <th></th> <th></th> <th></th> <th>Value (Å)</th> <th>Limit</th> <th>Limit</th>	Restraint	Resonances						Value (Å)	Limit	Limit
2   residue   2   HA   residue   2   HB1   2.777   4.177   1.632     3   residue   2   HB1   residue   2   HB2   2.793   3.275   2.2183     6   residue   2   HD#   residue   2   HB2   2.490   4.976   0.000     7   residue   2   HD#   residue   2   HB3   2.332   4.789   0.000     8   residue   2   HD#   residue   3   HB3   5.838   0.568     10   residue   3   HN   residue   3   HB2   2.974   3.569   2.379     12   residue   3   HB1   residue   3   HA   2.707   3.807   2.246     14   residue   3   HB1   residue   3   HD2   2.808   3.834   2.202     16   residue   3   HD2   2.473   4.066   2.201	1	residue	2	HA	residue	2	HN	2.613	3.136	2.090
3   residue   2   HA   residue   2   HB2   3.032   4.432   1.652     4   residue   2   HB2   residue   2   HN   2.779   3.275   2.183     6   residue   2   HD#   residue   2   HB2   2.480   4.976   0.000     7   residue   2   HD#   residue   2   HB1   2.332   4.789   0.000     8   residue   3   HN   residue   3   HB2   2.974   3.569   2.379     12   residue   3   HB1   residue   3   HA   2.707   3.807   1.607     14   residue   3   HB2   residue   3   HD2   2.804   3.403   2.202     17   residue   3   HB2   residue   3   HD2   1.607   1.877   3.777   1.777   3.777   1.777   3.777   1.777   1.777   3.777 <td>2</td> <td>residue</td> <td>2</td> <td>HA</td> <td>residue</td> <td>2</td> <td>HB1</td> <td>2.777</td> <td>4.177</td> <td>1.377</td>	2	residue	2	HA	residue	2	HB1	2.777	4.177	1.377
4   residue   2   HBI   residue   2   HBI   zesidue   3   HBI   zesidue   3   HBI   zesidue   3   HBI   residue   3   HBI   zesidue   4   HBI   zesidue   3   KBI	3	residue	2	HA	residue	2	HB2	3.032	4.432	1.632
5   residue   2   HB2   residue   2   HB2   2.480   4.976   0.000     6   residue   2   HD#   residue   2   HB1   2.332   4.788   0.000     8   residue   2   HD#   residue   3   HB1   2.354   4.789   0.000     9   residue   3   HN   residue   3   HB1   3.058   3.670   2.480     11   residue   3   HN   residue   3   HA   2.777   3.777   1.777     12   residue   3   HB1   residue   3.807   1.607     14   residue   3   HB1   residue   3.63   4.03   2.660   1.777     15   residue   3   HB1   residue   3.63   4.03   2.660   1.607     14   residue   3   HB1   residue   3.63   4.03   4.03   4.03   4.03   4.03 <td>4</td> <td>residue</td> <td>2</td> <td>HB1</td> <td>residue</td> <td>2</td> <td>HN</td> <td>2.771</td> <td>3.325</td> <td>2.217</td>	4	residue	2	HB1	residue	2	HN	2.771	3.325	2.217
	5	residue	2	HB2	residue	2	HN	2.729	3.275	2.183
7 residue 2 HB1 2.332 4.789 0.000   8 residue 2 HB7 residue 4 HB2 3.198 5.838 0.058   10 residue 3 HN residue 3 HB1 3.059 2.446   11 residue 3 HN residue 3 HB2 2.974 3.869 2.379   12 residue 3 HN residue 3 HA 2.777 3.807 1.607   14 residue 3 HB2 residue 3 HD21 2.800 3.560 2.446   16 residue 3 HB2 residue 3 HD21 3.028 3.834 2.222   17 residue 4 HA residue 4 HB1 residue 4 HB2 2.473 4.073 0.873   18 residue 4 HD1 residue 4 HB2 3.386 6.662 0.708   23 residue 4 HD1 r	6	residue	2	HD#	residue	2	HB2	2.480	4.976	0.000
8   residue   2   HA   2.324   4.789   0.000     9   residue   3   HN   residue   3   HB1   3.058   3.670   2.446     10   residue   3   HN   residue   3   HB2   2.974   3.569   2.379     12   residue   3   HN   residue   3   HA   2.707   3.807   1.607     14   residue   3   HB1   residue   3   HA   2.707   3.777   1.777     15   residue   3   HB1   residue   3   HD21   2.800   3.560   2.040     16   residue   3   HD22   residue   4   HB1   3.043   4.036   2.696     18   residue   4   HD1   residue   4   HB1   3.048   4.748   1.778     21   residue   4   HD1   residue   4   HD1   residue   4	7	residue	2	HD#	residue	2	HB1	2.332	4.798	0.000
9   residue   2   IE#   residue   3   HB2   3.198   5.838   0.558     10   residue   3   HN   residue   3   HB2   2.974   3.569   2.379     12   residue   3   HN   residue   3   HA   2.777   3.569   2.379     12   residue   3   HB1   residue   3   HA   2.777   3.577   1.777     15   residue   3   HB2   residue   3   HD21   3.028   3.834   2.222     17   residue   3   HD2   residue   4   HA   residue   4   HB1   3.048   4.073   0.0873     21   residue   4   HD1   residue   4   HB1   3.736   6.483   0.989     22   residue   4   HD1   residue   4   HB1   3.736   6.483   0.989     23   residue   4	8	residue	2	HD#	residue	2	HA	2.324	4.789	0.000
10 residue 3 HN residue 3 HB1 3.058 3.670 2.246  11 residue 3 HN residue 3 HB2 2.974 3.569 2.179  12 residue 3 HB1 residue 3 HA 2.717 3.260 2.174  13 residue 3 HB1 residue 3 HA 2.707 3.777 1.677  15 residue 3 HB1 residue 3 HA 2.707 3.777 1.777  15 residue 3 HB1 residue 3 HA 2.707 3.777 1.777  15 residue 3 HB2 residue 3 HD21 2.800 3.560 2.040  16 residue 3 HB2 residue 3 HD21 3.028 3.834 2.222  17 residue 3 HB2 residue 4 HB2 3.036 4.036 2.690  18 residue 4 HA residue 4 HB1 3.048 4.748 1.348  20 residue 4 HA residue 4 HB1 3.048 4.748 1.348  20 residue 4 HA residue 4 HB2 3.385 6.062 0.708  12 residue 4 HD1 residue 4 HB2 3.385 6.062 0.708  21 residue 4 HD1 residue 4 HB2 3.385 6.062 0.708  22 residue 4 HD1 residue 4 HB2 3.385 6.062 0.708  23 residue 4 HD1 residue 4 HB2 3.385 6.062 0.708  23 residue 4 HD1 residue 5 HA 2.221 2.666 1.777  25 residue 4 HD1 residue 5 HA 2.221 2.666 1.777  26 residue 4 HD1 residue 5 HA 2.221 2.666 1.777  26 residue 5 HN residue 5 HD# 3.251 5.901 0.061  27 residue 5 HN residue 5 HA 2.122 2.524 1.698  28 residue 5 HN residue 5 HA 2.074 3.209 2.139  29 residue 5 HN residue 5 HA 2.674 3.209 2.139  2003  30 residue 5 HN residue 5 HA 2.674 3.209 2.139  2003  31 residue 5 HN residue 5 HA 2.674 3.209 2.139  2003  31 residue 5 HN residue 5 HA 3.037 4.337 1.737  34 residue 5 HN residue 5 HA 3.037 4.337 1.737  34 residue 5 HN residue 6 HB1 3.129 4.255 2.003  35 residue 5 HN residue 6 HB2 2.904 4.748 0.0000  35 residue 5 HN residue 6 HD# 2.230 4.748 0.0000  36 residue 5 HN residue 6 HD# 2.240 4.748 0.492  307 residue 5 HN residue 6 HD# 2.304 4.923 2.944 1.962  337 residue 5 HN residue 6 HA 2.799 3.359 2.239  40 residue 6 HN residue 6 HB1 2.912 4.012 1.812  456 residue 6 HN residue 6 HB1 2.912 4.012 1.812  456 residue 6 HN residue 6	9	residue	2	HE#	residue	4	HB2	3.198	5.838	0.558
11 residue 3 HN residue 3 HA 2.774 3.569 2.379   12 residue 3 HB1 residue 3 HA 2.707 3.807 1.607   14 residue 3 HB1 residue 3 HA 2.707 3.807 1.607   15 residue 3 HB2 residue 3 HD21 2.800 3.560 2.040   16 residue 3 HD21 2.800 3.566 2.040   17 residue 3 HD21 2.800 3.566 2.040   18 residue 4 HA residue 4 HB1 3.048 4.748 1.348   20 residue 4 HD1 residue 4 HB2 3.335 6.062 0.708   21 residue 4 HD1 residue 4 HB2 3.335 6.062 1.777   24 residue 4 HD1 residue 5 HD4 3.221 2.665	10	residue	3	HN	residue	3	HB1	3.058	3.670	2.446
12   residue   3   HN   residue   3   HA   2.717   3.260   2.174     13   residue   3   HB1   residue   3   HA   2.777   3.777   1.777     15   residue   3   HB2   residue   3   HA   2.777   3.777   1.777     15   residue   3   HB2   residue   3   HB2   2.808   3.884   2.222     17   residue   3   HD21   s3.634   4.036   2.660   1.798     18   residue   4   HA   residue   4   HB1   3.736   6.448   0.987     21   residue   4   HD1   residue   4   HB2   2.473   4.073   0.873     22   residue   4   HD1   residue   4   HB2   2.473   4.073   0.875     23   residue   4   HD1   residue   3   HA   2.2665	11	residue	3	HN	residue	3	HB2	2.974	3.569	2.379
13   residue   3   HB1   residue   3   HA   2.707   3.807   1.607     14   residue   3   HB2   residue   3   HD21   2.800   3.560   2.040     16   residue   3   HD21   3.028   3.563   4.036   2.040     17   residue   3   HD21   3.028   3.563   4.036   2.696   1.798     18   residue   4   HA   residue   4   HA   3.363   4.036   4.648   1.798     20   residue   4   HD1   residue   4   HB1   3.048   4.748   1.348     20   residue   4   HD1   residue   4   HB2   3.335   6.062   0.0708     21   residue   4   HD1   residue   4   HA   2.212   2.665   1.777     25   residue   4   HD2   residue   5   HA   2.212 <td>12</td> <td>residue</td> <td>3</td> <td>HN</td> <td>residue</td> <td>3</td> <td>HA</td> <td>2.717</td> <td>3.260</td> <td>2.174</td>	12	residue	3	HN	residue	3	HA	2.717	3.260	2.174
14 residue 3 HB2 residue 3 HA 2.777 3.777 1.777   15 residue 3 HB2 residue 3 HD21 3.028 3.854 2.222   17 residue 3 HD21 s.028 3.854 2.222   17 residue 3 HD12 residue 4.406 2.660 1.798   19 residue 4 HA residue 4.4181 3.048 4.748 1.348   20 residue 4 HD1 residue 4 HB2 2.473 4.073 0.873   21 residue 4 HD1 residue 4 HB2 2.473 4.073 0.873   22 residue 4 HD1 residue 3 HA 2.221 2.665 1.777   25 residue 4 HD2 residue 5 HA 2.674 3.209 2.122 2.524 1.698   28 residue 5 HA 2.674 3.205 2.0	13	residue	3	HB1	residue	3	HA	2.707	3.807	1.607
15   residue   3   HB1   residue   3   HD21   2.800   3.560   2.242     17   residue   3   HD22   residue   3   HA   3.363   4.036   2.222     17   residue   3   HA   residue   4   HA   2.247   2.696   1.798     18   residue   4   HA   residue   4   HB1   3.048   4.748   1.348     20   residue   4   HD1   residue   4   HB1   3.736   6.483   0.989     21   residue   4   HD1   residue   3.885   6.062   0.708     22   residue   4   HD1   residue   3.14   2.212   2.665   1.777     25   residue   4   HD2   residue   3.41A   2.122   2.524   1.698     28   residue   5   HN   residue   5   HB1   3.129   4.255   2	14	residue	3	HB2	residue	3	HA	2.777	3.777	1.777
16   residue   3   HD21   3.028   3.834   2.22     17   residue   3   HN   residue   3   HA   3.63   4.03     18   residue   4   HA   residue   4   HB1   3.048   4.748   1.348     20   residue   4   HA   residue   4   HB2   2.473   4.073   0.873     21   residue   4   HD1   residue   4   HB2   3.385   6.062   0.708     22   residue   4   HD1   residue   4   HB2   7.65   5.518   2.012     24   residue   4   HD1   residue   2.112   2.665   1.777     25   residue   4   HD2   residue   5   HD#   3.251   5.901   0.601     27   residue   5   HN   residue   5   HB1   3.252   2.033     30   residue	15	residue	3	HB1	residue	3	HD21	2.800	3.560	2.040
17 residue 3 HD22 residue 2 HA 2.247 2.696 1.798   18 residue 4 HA residue 4 HB1 3.048 4.748 1.348   20 residue 4 HA residue 4 HB1 3.736 6.483 0.989   21 residue 4 HD1 residue 4 HB2 3.385 6.062 0.0708   23 residue 4 HD1 residue 3 HA 2.21 2.665 1.777   25 residue 4 HD1 residue 5 HA 2.221 2.665 1.777   26 residue 5 HN residue 5 HA 2.121 2.665 1.777   26 residue 5 HN residue 5 HA 2.122 2.524 1.698   28 residue 5 HN residue 5 HA 2.674 3.209 2.139   29 residue 5 HN <td>16</td> <td>residue</td> <td>3</td> <td>HB2</td> <td>residue</td> <td>3</td> <td>HD21</td> <td>3.028</td> <td>3.834</td> <td>2.222</td>	16	residue	3	HB2	residue	3	HD21	3.028	3.834	2.222
$ \begin{array}{ c c c c c c c c c c c c c c c c c c c$	17	residue	3	HD22	residue	3	HA	3.363	4.036	2.690
19 residue 4 HA residue 4 HB1 3.048 4.748 1.348   20 residue 4 HD1 residue 4 HB2 2.473 4.073 0.873   21 residue 4 HD1 residue 4 HB1 3.736 6.483 0.989   22 residue 4 HD1 residue 4 HB2 3.385 6.062 0.708   23 residue 4 HD1 residue 3 HA 3.765 5.518 2.012   24 residue 4 HD1 residue 5 HD7# 3.251 5.901 0.601   27 residue 5 HN residue 5 HB1 3.129 4.2255 2.003   30 residue 5 HN residue 5 HB1 1.129 4.255 2.003   31 residue 5 HB2 residue 5 HD# 2.290 4.748 0.000   32 residue 5 <	18	residue	3	HN	residue	2	HA	2.247	2.696	1.798
$ \begin{array}{ c c c c c c c c c c c c c c c c c c c$	19	residue	4	HA	residue	4	HB1	3.048	4.748	1.348
21 residue 4 HD1 residue 4 HB2 3.385 6.062 0.708   22 residue 4 HG1 residue 4 HB2 3.385 6.062 0.708   23 residue 4 HD1 residue 3 HA 2.221 2.665 1.777   25 residue 4 HD1 residue 5 HD# 3.251 5.901 0.601   27 residue 5 HN residue 5 HD 2.524 1.698   28 residue 5 HN residue 5 HB1 3.129 4.255 2.003   30 residue 5 HN residue 5 HB1 3.129 4.255 2.003   31 residue 5 HB1 residue 5 HB2 2.641 3.669 1.613   31 residue 5 HB1 residue 5 HD4 3.275 4.575 1.975   33 residue 5 HB1 re	20	residue	4	HA	residue	4	HB2	2.473	4.073	0.873
$\begin{array}{cccccccccccccccccccccccccccccccccccc$	21	residue	4	HD1	residue	4	HB1	3.736	6.483	0.989
23 residue 4 HG1 residue 3 HA 3.765 5.518 2.012   24 residue 4 HD1 residue 3 HA 2.221 2.665 1.777   25 residue 4 HD2 residue 5 HD# 3.296 5.955 0.637   26 residue 4 HD2 residue 5 HD# 3.251 5.901 0.601   27 residue 5 HN residue 5 HB4 2.129 2.524 1.698   28 residue 5 HN residue 5 HB1 3.129 4.255 2.003   30 residue 5 HN residue 5 HD# 2.290 4.748 0.000   31 residue 5 HB1 residue 5 HD# 2.301 4.337 1.737   34 residue 5 HB1 residue 5 HD# 2.391 4.869 0.000   35 residue 5	22	residue	4	HD1	residue	4	HB2	3.385	6.062	0.708
24   residue   4   HD1   residue   2   HE#   3.296   5.955   0.637     25   residue   4   HD2   residue   3   HA   2.121   2.665   0.631     26   residue   4   HD2   residue   3   HA   2.122   2.524   1.698     28   residue   5   HN   residue   5   HA   2.674   3.209   2.139     29   residue   5   HN   residue   5   HB   2.674   3.669   1.613     31   residue   5   HA   residue   5   HB   2.0641   3.669   1.613     31   residue   5   HB   residue   5   HA   3.037   4.737   1.737     34   residue   5   HB1   residue   5   HD#   2.391   4.869   0.000     35   residue   5   HN   residue   5	23	residue	4	HG1	residue	4	HA	3.765	5.518	2.012
$ \begin{array}{cccccccccccccccccccccccccccccccccccc$	24	residue	4	HD1	residue	3	HA	2.221	2.665	1.777
$ \begin{array}{cccccccccccccccccccccccccccccccccccc$	25	residue	4	HD1	residue	2	HE#	3.296	5.955	0.637
$ \begin{array}{cccccccccccccccccccccccccccccccccccc$	26	residue	4	HD2	residue	5	HD#	3.251	5.901	0.601
28   residue   5   HN   residue   5   HA   2.674   3.209   2.139     29   residue   5   HN   residue   5   HB1   2.674   3.209   2.139     30   residue   5   HN   residue   5   HB1   2.641   3.669   1.613     31   residue   5   HB1   residue   5   HA   3.275   4.575   1.975     33   residue   5   HB2   residue   5   HA   3.037   4.337   1.737     34   residue   5   HB1   residue   5   HD#   2.436   4.923   0.000     35   residue   5   HN   residue   4   HA   2.436   4.923   0.000     36   residue   5   HN   residue   4   HA   2.436   2.944   1.962     37   residue   6   HN   residue   6   H	27	residue	4	HD2	residue	3	HA	2.122	2.524	1.698
29   residue   5   HN   residue   5   HB1   3.129   4.255   2.003     30   residue   5   HN   residue   5   HB2   2.641   3.669   1.613     31   residue   5   HB1   residue   5   HB4   3.275   4.575   1.975     33   residue   5   HB2   residue   5   HA   3.275   4.575   1.975     34   residue   5   HB2   residue   5   HD#   2.436   4.923   0.000     35   residue   5   HN   residue   4   HB1   3.237   3.884   2.590     37   residue   5   HN   residue   4   HD2   3.046   3.655   2.437     38   residue   6   HN   residue   6   HA   2.799   3.359   2.239     40   residue   6   HN   residue   6 <t< td=""><td>28</td><td>residue</td><td>5</td><td>HN</td><td>residue</td><td>5</td><td>HA</td><td>2.674</td><td>3.209</td><td>2.139</td></t<>	28	residue	5	HN	residue	5	HA	2.674	3.209	2.139
30   residue   5   HN   residue   5   HB2   2.641   3.669   1.613     31   residue   5   HA   residue   5   HD   #   2.290   4.748   0.000     32   residue   5   HB1   residue   5   HA   3.037   4.748   0.000     33   residue   5   HB2   residue   5   HA   3.037   4.337   1.737     34   residue   5   HB1   residue   5   HD   2.436   4.923   0.000     35   residue   5   HN   residue   4   HB1   3.237   3.884   2.590     36   residue   5   HN   residue   4   HD2   3.046   3.655   2.437     39   residue   6   HN   residue   6   HB1   2.868   3.742   1.994     41   residue   6   HA   residue	29	residue	5	HN	residue	5	HB1	3.129	4.255	2.003
31 residue 5 HA residue 5 HD# 2.290 4.748 0.000   32 residue 5 HB1 residue 5 HA 3.275 4.575 1.975   33 residue 5 HB2 residue 5 HD 2.436 4.923 0.000   35 residue 5 HB2 residue 5 HD# 2.391 4.869 0.000   36 residue 5 HN residue 4 HB1 3.237 3.884 2.590   37 residue 5 HN residue 4 HD2 3.046 3.655 2.437   38 residue 6 HN residue 6 HB1 2.868 3.742 1.994   41 residue 6 HN residue 6 HB1 2.868 3.742 1.994   41 residue 6 HN residue 6 HG1 3.121 3.745 2.497   43 residue 6 HA<	30	residue	5	HN	residue	5	HB2	2.641	3.669	1.613
$\begin{array}{c ccccccccccccccccccccccccccccccccccc$	31	residue	5	HA	residue	5	HD#	2.290	4.748	0.000
$ \begin{array}{c ccccccccccccccccccccccccccccccccccc$	32	residue	5	HB1	residue	5	HA	3.275	4.575	1.975
$\begin{array}{c ccccccccccccccccccccccccccccccccccc$	33	residue	5	HB2	residue	5	HA	3.037	4.337	1.737
$\begin{array}{c ccccccccccccccccccccccccccccccccccc$	34	residue	5	HB1	residue	5	HD#	2.436	4.923	0.000
36 residue 5 HN residue 4 HB1 3.237 3.884 2.590   37 residue 5 HN residue 4 HD2 3.046 3.655 2.437   38 residue 6 HN residue 6 HA 2.799 3.359 2.239   40 residue 6 HN residue 6 HB1 2.868 3.742 1.994   41 residue 6 HN residue 6 HB2 3.210 4.152 2.268   42 residue 6 HA residue 6 HG1 3.121 3.745 2.497   43 residue 6 HA residue 6 HB1 2.912 4.012 1.812   45 residue 6 HA residue 5 HA 2.385 2.862 1.908   47 residue 7 HN residue 7 HA 2.265 2.718 1.812   48 residue 7 HN	35	residue	5	HB2	residue	5	HD#	2.391	4.869	0.000
37 residue 5 HN residue 4 HA 2.453 2.944 1.962   38 residue 5 HN residue 4 HD2 3.046 3.655 2.437   39 residue 6 HN residue 6 HB1 2.868 3.742 1.994   41 residue 6 HN residue 6 HB2 3.210 4.152 2.268   42 residue 6 HN residue 6 HG1 3.121 3.745 2.497   43 residue 6 HA residue 6 HG1 2.912 4.012 1.812   44 residue 6 HA residue 6 HB1 2.912 4.012 1.812   45 residue 6 HA residue 6 HB2 2.960 4.060 1.860   46 residue 7 HN residue 7 HA 2.265 2.718 1.812   48 residue 7 HN <td>36</td> <td>residue</td> <td>5</td> <td>HN</td> <td>residue</td> <td>4</td> <td>HB1</td> <td>3.237</td> <td>3.884</td> <td>2.590</td>	36	residue	5	HN	residue	4	HB1	3.237	3.884	2.590
38   residue   5   HN   residue   4   HD2   3.046   3.655   2.437     39   residue   6   HN   residue   6   HA   2.799   3.359   2.239     40   residue   6   HN   residue   6   HB1   2.868   3.742   1.994     41   residue   6   HN   residue   6   HB2   3.210   4.152   2.268     42   residue   6   HA   residue   6   HG1   3.121   3.745   2.497     43   residue   6   HA   residue   6   HG1   2.912   4.012   1.812     45   residue   6   HA   residue   6   HB2   2.960   4.060   1.860     46   residue   7   HN   residue   7   HA   2.265   2.718   1.812     47   residue   7   HN   residue   7   H	37	residue	5	HN	residue	4	HA	2.453	2.944	1.962
39 residue 6 HN residue 6 HA 2.799 3.359 2.239   40 residue 6 HN residue 6 HB1 2.868 3.742 1.994   41 residue 6 HN residue 6 HB1 2.868 3.742 1.994   41 residue 6 HN residue 6 HB1 2.210 4.152 2.268   42 residue 6 HA residue 6 HG1 3.121 3.745 2.497   43 residue 6 HA residue 6 HB1 2.912 4.012 1.812   45 residue 6 HA residue 5 HA 2.385 2.862 1.908   47 residue 7 HN residue 7 HA 2.265 2.718 1.812   48 residue 7 HN residue 7 HB1 2.892 3.870 1.914   49 residue 7 HN	38	residue	5	HN	residue	4	HD2	3.046	3.655	2.437
40 residue 6 HN residue 6 HB1 2.868 3.742 1.994   41 residue 6 HN residue 6 HB2 3.210 4.152 2.268   42 residue 6 HN residue 6 HG1 3.121 3.745 2.497   43 residue 6 HA residue 6 HG1 2.935 3.522 2.348   44 residue 6 HA residue 6 HB1 2.912 4.012 1.812   45 residue 6 HA residue 5 HA 2.385 2.862 1.908   47 residue 7 HN residue 7 HA 2.265 2.718 1.812   48 residue 7 HN residue 7 HB1 2.892 3.870 1.914   49 residue 7 HN residue 7 HB2 3.259 4.779 1.739   50 residue 7 HA <td>39</td> <td>residue</td> <td>6</td> <td>HN</td> <td>residue</td> <td>6</td> <td>HA</td> <td>2.799</td> <td>3.359</td> <td>2.239</td>	39	residue	6	HN	residue	6	HA	2.799	3.359	2.239
41 residue 6 HN residue 6 HB2 3.210 4.152 2.268   42 residue 6 HN residue 6 HG1 3.121 3.745 2.497   43 residue 6 HA residue 6 HG1 2.935 3.522 2.348   44 residue 6 HA residue 6 HB1 2.912 4.012 1.812   45 residue 6 HA residue 6 HB2 2.960 4.060 1.860   46 residue 6 HN residue 5 HA 2.385 2.862 1.908   47 residue 7 HN residue 7 HA 2.265 2.718 1.812   48 residue 7 HN residue 7 HB1 2.892 3.870 1.914   49 residue 7 HN residue 7 HB2 3.259 4.779 1.739   50 residue 7 HA <td>40</td> <td>residue</td> <td>6</td> <td>HN</td> <td>residue</td> <td>6</td> <td>HB1</td> <td>2.868</td> <td>3.742</td> <td>1.994</td>	40	residue	6	HN	residue	6	HB1	2.868	3.742	1.994
42 residue 6 HN residue 6 HG1 3.121 3.745 2.497   43 residue 6 HA residue 6 HG1 2.935 3.522 2.348   44 residue 6 HA residue 6 HB1 2.912 4.012 1.812   45 residue 6 HA residue 6 HB2 2.960 4.060 1.860   46 residue 6 HN residue 5 HA 2.385 2.862 1.908   47 residue 7 HN residue 7 HA 2.265 2.718 1.812   48 residue 7 HN residue 7 HB1 2.892 3.870 1.914   49 residue 7 HN residue 7 HB2 3.259 4.779 1.739   50 residue 7 HA residue 7 HB2 2.907 4.007 1.807   51 residue 7 HA <td>41</td> <td>residue</td> <td>6</td> <td>HN</td> <td>residue</td> <td>6</td> <td>HB2</td> <td>3.210</td> <td>4.152</td> <td>2.268</td>	41	residue	6	HN	residue	6	HB2	3.210	4.152	2.268
43 residue 6 HA residue 6 HG1 2.935 3.522 2.348   44 residue 6 HA residue 6 HB1 2.912 4.012 1.812   45 residue 6 HA residue 6 HB2 2.960 4.060 1.860   46 residue 6 HN residue 5 HA 2.385 2.862 1.908   47 residue 7 HN residue 7 HA 2.265 2.718 1.812   48 residue 7 HN residue 7 HB1 2.892 3.870 1.914   49 residue 7 HN residue 7 HB2 3.259 4.779 1.739   50 residue 7 HA residue 7 HB2 3.923 1.933   51 residue 7 HA residue 7 HB2 2.907 4.007 1.807   52 residue 7 HA residue </td <td>42</td> <td>residue</td> <td>6</td> <td>HN</td> <td>residue</td> <td>6</td> <td>HG1</td> <td>3.121</td> <td>3.745</td> <td>2.497</td>	42	residue	6	HN	residue	6	HG1	3.121	3.745	2.497
44 residue 6 HA residue 6 HB1 2.912 4.012 1.812   45 residue 6 HA residue 6 HB2 2.960 4.060 1.860   46 residue 6 HN residue 5 HA 2.385 2.862 1.908   47 residue 7 HN residue 7 HA 2.265 2.718 1.812   48 residue 7 HN residue 7 HB1 2.892 3.870 1.914   49 residue 7 HN residue 7 HB2 3.259 4.779 1.739   50 residue 7 HN residue 7 HB2 3.421 5.105 1.737   51 residue 7 HA residue 7 HB1 2.893 3.993 1.793   52 residue 7 HA residue 7 HB2 2.907 4.007 1.807   53 residue 7 HG# <td>43</td> <td>residue</td> <td>6</td> <td>HA</td> <td>residue</td> <td>6</td> <td>HGI</td> <td>2.935</td> <td>3.522</td> <td>2.348</td>	43	residue	6	HA	residue	6	HGI	2.935	3.522	2.348
45 residue 6 HA residue 6 HB2 2.960 4.060 1.860   46 residue 6 HN residue 5 HA 2.385 2.862 1.908   47 residue 7 HN residue 7 HA 2.265 2.718 1.812   48 residue 7 HN residue 7 HB1 2.892 3.870 1.914   49 residue 7 HN residue 7 HB2 3.259 4.779 1.739   50 residue 7 HN residue 7 HB1 2.893 3.993 1.773   51 residue 7 HA residue 7 HB2 2.907 4.007 1.807   52 residue 7 HG# residue 7 HB2 2.907 4.007 1.807   53 residue 7 HG# residue 8 HA1 2.748 3.498 1.998   55 residue 8 HN </td <td>44</td> <td>residue</td> <td>6</td> <td>HA</td> <td>residue</td> <td>6</td> <td>HBI</td> <td>2.912</td> <td>4.012</td> <td>1.812</td>	44	residue	6	HA	residue	6	HBI	2.912	4.012	1.812
46 residue 6 HN residue 5 HA 2.385 2.862 1.908   47 residue 7 HN residue 7 HA 2.265 2.718 1.812   48 residue 7 HN residue 7 HB1 2.892 3.870 1.914   49 residue 7 HN residue 7 HB2 3.259 4.779 1.739   50 residue 7 HN residue 7 HB2 3.421 5.105 1.737   51 residue 7 HA residue 7 HB1 2.893 3.993 1.793   52 residue 7 HA residue 7 HB2 2.907 4.007 1.807   53 residue 7 HG# residue 7 HA 3.080 4.696 1.464   54 residue 8 HN residue 8 HA2 2.930 3.716 2.144   56 residue 8 HN <td>45</td> <td>residue</td> <td>6</td> <td>HA</td> <td>residue</td> <td>6</td> <td>HB2</td> <td>2.960</td> <td>4.060</td> <td>1.860</td>	45	residue	6	HA	residue	6	HB2	2.960	4.060	1.860
47 residue 7 HN residue 7 HA 2.265 2.718 1.812   48 residue 7 HN residue 7 HB1 2.892 3.870 1.914   49 residue 7 HN residue 7 HB2 3.259 4.779 1.739   50 residue 7 HN residue 7 HB2 3.421 5.105 1.737   51 residue 7 HA residue 7 HB1 2.893 3.993 1.793   52 residue 7 HA residue 7 HB2 2.907 4.007 1.807   53 residue 7 HG# residue 7 HA 3.080 4.696 1.464   54 residue 8 HN residue 8 HA1 2.748 3.498 1.998   55 residue 8 HN residue 8 HA2 2.930 3.716 2.144   56 residue 8 HN <td>46</td> <td>residue</td> <td>6</td> <td>HN</td> <td>residue</td> <td>5</td> <td>HA</td> <td>2.385</td> <td>2.862</td> <td>1.908</td>	46	residue	6	HN	residue	5	HA	2.385	2.862	1.908
48 residue 7 HN residue 7 HB1 2.892 3.870 1.914   49 residue 7 HN residue 7 HB2 3.259 4.779 1.739   50 residue 7 HN residue 7 HB2 3.259 4.779 1.739   50 residue 7 HN residue 7 HG# 3.421 5.105 1.737   51 residue 7 HA residue 7 HB1 2.893 3.993 1.793   52 residue 7 HA residue 7 HB2 2.907 4.007 1.807   53 residue 7 HG# residue 7 HA 3.080 4.696 1.464   54 residue 8 HN residue 8 HA1 2.748 3.498 1.998   55 residue 8 HN residue 8 HA2 2.930 3.716 2.144   56 residue 8 HN </td <td>47</td> <td>residue</td> <td>7</td> <td>HN</td> <td>residue</td> <td>7</td> <td>HA UD1</td> <td>2.265</td> <td>2.718</td> <td>1.812</td>	47	residue	7	HN	residue	7	HA UD1	2.265	2.718	1.812
49 residue 7 HN residue 7 HB2 3.259 4.779 1.739   50 residue 7 HN residue 7 HG# 3.421 5.105 1.737   51 residue 7 HA residue 7 HB1 2.893 3.993 1.793   52 residue 7 HA residue 7 HB2 2.907 4.007 1.807   53 residue 7 HG# residue 7 HA 3.080 4.696 1.464   54 residue 8 HN residue 8 HA1 2.748 3.498 1.998   55 residue 8 HN residue 8 HA2 2.930 3.716 2.144   56 residue 8 HN residue 6 HA 2.468 2.962 1.974   57 residue 9 HN residue 9 HA1 2.417 3.817 1.017   58 residue 9 HN <td>48</td> <td>residue</td> <td>/</td> <td>HN</td> <td>residue</td> <td>/</td> <td>HBI</td> <td>2.892</td> <td>3.870</td> <td>1.914</td>	48	residue	/	HN	residue	/	HBI	2.892	3.870	1.914
50 residue 7 HN residue 7 HG# 3.421 5.105 1.737   51 residue 7 HA residue 7 HB1 2.893 3.993 1.793   52 residue 7 HA residue 7 HB2 2.907 4.007 1.807   53 residue 7 HG# residue 7 HA 3.080 4.696 1.464   54 residue 8 HN residue 8 HA1 2.748 3.498 1.998   55 residue 8 HN residue 8 HA2 2.930 3.716 2.144   56 residue 8 HN residue 6 HA 2.468 2.962 1.974   57 residue 9 HN residue 9 HA1 2.417 3.817 1.017   58 residue 9 HN residue 9 HA2 3.336 4.836 1.836   59 residue 9 HN <td>49</td> <td>residue</td> <td>/</td> <td>HN</td> <td>residue</td> <td>/</td> <td>HB2</td> <td>3.259</td> <td>4.//9</td> <td>1.739</td>	49	residue	/	HN	residue	/	HB2	3.259	4.//9	1.739
51 residue / HA residue / HB1 2.893 3.993 1.793   52 residue 7 HA residue 7 HB2 2.907 4.007 1.807   53 residue 7 HG# residue 7 HA 3.080 4.696 1.464   54 residue 8 HN residue 8 HA1 2.748 3.498 1.998   55 residue 8 HN residue 8 HA2 2.930 3.716 2.144   56 residue 8 HN residue 6 HA 2.468 2.962 1.974   57 residue 9 HN residue 9 HA1 2.417 3.817 1.017   58 residue 9 HN residue 9 HA2 3.336 4.836 1.836   59 residue 9 HN residue 7 HA 3.205 3.846 2.564	50	residue	/		residue	/	HG#	3.421	5.105	1./5/
32 residue / HA residue / HB2 2.90/ 4.00/ 1.80/   53 residue 7 HG# residue 7 HA 3.080 4.696 1.464   54 residue 8 HN residue 8 HA1 2.748 3.498 1.998   55 residue 8 HN residue 8 HA2 2.930 3.716 2.144   56 residue 8 HN residue 6 HA 2.468 2.962 1.974   57 residue 9 HN residue 9 HA1 2.417 3.817 1.017   58 residue 9 HN residue 9 HA2 3.336 4.836 1.836   59 residue 9 HN residue 7 HA 3.205 3.846 2.564	51	residue	/		residue	/		2.893	3.993	1./93
53 residue 7 FIGH Festure 7 FIA 5.080 4.096 1.464   54 residue 8 HN residue 8 HA1 2.748 3.498 1.998   55 residue 8 HN residue 8 HA2 2.930 3.716 2.144   56 residue 8 HN residue 6 HA 2.468 2.962 1.974   57 residue 9 HN residue 9 HA1 2.417 3.817 1.017   58 residue 9 HN residue 9 HA2 3.336 4.836 1.836   59 residue 9 HN residue 7 HA 3.205 3.846 2.564	52	residue	7	ПА ЦС#	residue	/ 7	нв2 ца	2.907	4.00/	1.80/
54 residue 6 FIN residue 8 HA1 2.748 5.498 1.998   55 residue 8 HN residue 8 HA2 2.930 3.716 2.144   56 residue 8 HN residue 6 HA 2.468 2.962 1.974   57 residue 9 HN residue 9 HA1 2.417 3.817 1.017   58 residue 9 HN residue 9 HA2 3.336 4.836 1.836   59 residue 9 HN residue 7 HA 3.205 3.846 2.564	55	residue	/	ПU# UN	residue	/		3.080	4.090	1.404
55 residue 6 FIN residue 8 HA2 2.950 5.716 2.144   56 residue 8 HN residue 6 HA 2.468 2.962 1.974   57 residue 9 HN residue 9 HA1 2.417 3.817 1.017   58 residue 9 HN residue 9 HA2 3.336 4.836 1.836   59 residue 9 HN residue 7 HA 3.205 3.846 2.564	54	residue	ð		residue	ð		2.748	5.498 2.716	1.998
50 residue 6 HN residue 6 HA 2.406 2.902 1.974   57 residue 9 HN residue 9 HA1 2.417 3.817 1.017   58 residue 9 HN residue 9 HA2 3.336 4.836 1.836   59 residue 9 HN residue 7 HA 3.205 3.846 2.564	55	residue	ð	IIN HN	residue	ð 6	ПАД НА	2.930	3./10	2.144
57   residue   9   HN   residue   9   HA1   2.417   5.617   1.017     58   residue   9   HN   residue   9   HA2   3.336   4.836   1.836     59   residue   9   HN   residue   7   HA   3.205   3.846   2.564	50	residue	0	HN HN	residue	0		2.408	2.902	1.9/4
50 residue 0 HN residue 7 HA 2 2.50 4.600 1.800	50	residue	9 0	HN HN	residue	9		2.41/	5.01/ 1.024	1.01/
	50	residue	9 0	HN	residue	ש ד	HA2	3.330	4.030	1.030 2.564

Table S6. Distance Restraints for the linear NPF peptide.

							0	Upper	
Restraint	Resonances						Value (Å)	Limit	Lower Limit
1	residue	1	HN	residue	1	HB1	2.313	3.426	1.200
2	residue	1	HN	residue	1	HB2	2.610	4.032	1.188
3	residue	1	HA	residue	1	HB1	2.719	3.863	1.575
4	residue	1	HA	residue	1	HB2	2.837	4.104	1.570
5	residue	1	HA	residue	1	HD#	2.490	4.988	0.000
6	residue	1	HE#	residue	1	HA	3.427	6.112	0.742
7	residue	1	HN	residue	1	HA	2.520	3.024	2.016
8	residue	1	HB1	residue	1	HD#	2.330	4.796	0.000
9	residue	1	HB2	residue	1	HD#	2.364	4.837	0.000
10	residue	1	HE#	residue	1	HB1	3.329	6.095	0.563
11	residue	1	HE#	residue	1	HB2	3.476	6.271	0.681
12	residue	1	HN	residue	1	HD#	2.909	5.491	0.327
13	residue	1	HB1	residue	2	HN	2.879	3.605	2.153
14	residue	1	HB2	residue	2	HN	2.939	4.939	2.351
15	residue	1	HB2	residue	2	HD22	3.898	5.128	2.668
16	residue	1	HB1	residue	2	HD22	3.635	5.112	2.158
17	residue	1	HA	residue	2	HN	2.904	3.585	2.223
18	residue	1	HN	residue	2	HN	2.128	2.536	1.702
19	residue	1	HN	residue	5	HB1	3.683	5.020	2.346
20	residue	1	HN	residue	5	HB2	3.774	5.179	2.369
21	residue	1	HN	residue	8	HA2	2.583	3.200	1.966
22	residue	1	HN	residue	8	HAI	2.320	3.284	1.356
23	residue	2	HB#	residue	l	HD#	3.185	6.022	0.348
24	residue	2	HB#	residue	2	HD22	2.658	3.790	1.526
25	residue	2	HB2	residue	2	HD21	3.034	5.141	1.927
26	residue	2	HBI	residue	2	HD21	3.318	4.882	1.754
27	residue	2	HBI	residue	2	HD22	2.695	3.834	1.556
28	residue	2	HB#	residue	2	HD22	2.319	3.783	0.855
29	residue	2	HN	residue	2	HB#	2.375	3.850	0.900
30	residue	2	HA	residue	2	HD21	3.315	4.528	2.102
31	residue	2	HA	residue	2	HD22	3.553	5.024	2.082
32	residue	2	HN	residue	2	HBI	2.730	3.526	1.934
33	residue	2		residue	2		2./10	3.752	1.008
24	residue	2		residue	2	НА	2.455	2.940	1.904
25	residue	2	HB2 UD1	residue	2		2.004	5.897	1.431
33	residue	2		residue	2		2.001	4.137	1.003
30	residue	2	пD22 uD2	residue	2 5	ID21	1.720	1.920	1.570
37	residue	2	IID2 IID1	residue	5		3.975	0.270	2.080
30	residue	2	HN	residue	5	HC#	3.430	4.973	2.099
40	residue	2	HD2	residue	2	HΔ	2 108	3 360	1.901
-+0 	residue	3	HD1	residue	2	HA	2.400	3 278	1.126
42	residue	3	HD?	residue	2	HB1	2.232	3 824	1 340
43	residue	3	HD2	residue	2	HB?	2.012	3 947	1.540
43	residue	3	HGI	residue	$\frac{2}{2}$	HB#	3 302	4 962	1 642
45	residue	3	HD1	residue	2	HB1	3 189	4 077	2 301
46	residue	3	HD1	residue	2	HB2	3 201	4 041	2.301
47	residue	ĩ	HG2	residue	รี	HA	3 671	4 905	2.437
48	residue	3	HG1	residue	ĩ	HA	3 128	4 254	2.002
49	residue	3 3	HD1	residue	ĩ	HB1	3 251	4 101	2.401
50	residue	3	HD2	residue	3 3	HB1	3 448	4 338	2.558
51	residue	3	HG2	residue	3	HB2	2 479	2.975	1 983
52	residue	3	HB2	residue	3	HB1	2.356	3.827	1.885
53	residue	3	HG2	residue	3	HD2	2.384	3.461	1.307
54	residue	3	HG1	residue	3	HD2	2.711	3 853	1 569
55	residue	3	HA	residue	3	HB2	2.639	3.667	1.611
56	residue	3	HG1	residue	3	HB2	2.597	3.116	2.078

Table S7. Distance Restraints for cNPF1.

57	residue	3	HD2	residue	3	HB2	3.086	4.003	2.169
58	residue	3	HG2	residue	3	HD1	2.804	3.365	2.243
59	residue	3	HA	residue	3	HB1	2.208	3.650	0.766
	residue	6	HB1	residue	3	HA			
60	residue	3	HG1	residue	3	HD1	2.414	3.447	1.381
61	residue	3	HD2	residue	4	HN	3.145	4.374	1.916
62	residue	3	HD1	residue	4	HN	3.756	5.157	2.355
63	residue	3	HD2	residue	4	HD#	3.436	6.223	0.649
64	residue	3	HG2	residue	4	HN	3.518	4.772	2.264
65	residue	4	HB2	residue	2	HD22	3.830	7.096	0.564
66	residue	4	HB2	residue	2	HD21	3.687	5.924	1.450
67	residue	4	HD#	residue	2	HB2	3.450	6.240	0.660
68	residue	4	HN	residue	2	HB1	3.572	4.586	2.558
69	residue	4	HN	residue	2	HB2	3.730	6.576	2.884
70	residue	4	HN	residue	3	HB2	3.334	4.401	2.267
71	residue	4	HD#	residue	3	HB2	2.983	5.630	0.336
72	residue	4	HN	residue	3	HA	2.338	3.536	1.140
73	residue	4	HN	residue	4	HA	2.432	3.068	1.796
74	residue	4	HB1	residue	4	HA	3.003	4.304	1.702
75	residue	4	HB2	residue	4	HA	2.805	4.066	1.544
76	residue	4	HB2	residue	4	HN	2.624	3.699	1.549
77	residue	4	HB1	residue	4	HN	3.127	4.252	2.002
78	residue	4	HB2	residue	4	HE#	3.307	6.268	0.346
79	residue	4	HB1	residue	4	HE#	3.618	6.642	0.594
80	residue	4	HD#	residue	4	HB2	2.248	4.898	-0.402
81	residue	4	HD#	residue	4	HB1	2.442	5.130	-0.246
82	residue	4	HD#	residue	4	HN	3.055	5.666	0.444
83	residue	4	HD#	residue	4	HA	2.386	4.863	-0.091
84	residue	4	HB1	residue	5	HN	3.337	4.204	1.137
85	residue	4	HB2	residue	5	HN	3.147	3.976	0.947
86	residue	4	HA	residue	5	HN	2.878	3.704	2.252
87	residue	4	HN	residue	5	HN	2.401	2.931	1.871
88	residue	5	HG#	residue	2	HD21	3.393	5.172	1.614
89	residue	5	HG#	residue	2	HD22	3.554	5.365	1.743
90	residue	5	HB1	residue	2	HN	3.062	3.874	2.250
91	residue	5	HB2	residue	2	HN	3.127	5.862	2.392
92	residue	5	HB1	residue	2	HD21	3.609	6.331	2.887
93	residue	5	HB1	residue	2	HD22	3.941	6.729	3.153
94	residue	5	HB1	residue	2	HB1	3.201	4.441	1.961
95	residue	5	HB1	residue	2	HB2	3.161	4.443	1.879
96	residue	5	HG#	residue	2	HD22	3.877	5.652	2.102
97	residue	5	HG#	residue	2	HD21	3.587	5.304	1.870
98	residue	5	HN	residue	3	HA	3.260	4.312	2.208
99	residue	5	HB2	residue	5	HN	2.850	3.520	2.180
100	residue	5	HA	residue	5	HG#	3.569	5.283	1.855
101	residue	5	HB2	residue	5	HA	2.620	4.044	1.196
102	residue	5	HBI	residue	5	HA	3.016	4.519	1.513
103	residue	5	HN	residue	5	HG#	2.984	4.581	1.387
104	residue	5	HN	residue	5	HG#	2.868	4.442	1.294
105	residue	5	HBI	residue	5	HN	2.487	3.034	1.940
106	residue	5	HA	residue	5	HN	2.465	2.958	1.972
107	residue	5	HA	residue	5	HG#	2.638	4.216	1.060
108	residue	5	HA UD1	residue	6	HN	2.600	3.570	1.630
109	residue	5	HBI	residue	6	HN	3.107	4.078	2.136
110	residue	5	HB2	residue	6	HN	3.098	4.168	2.028
111	residue	2	HG#	residue	8	HN	3.583	5.300	1.866
112	residue	6	HN LID2	residue	2	HA	3.330	5.896	0.764
115	residue	6		residue	5	HA UD1	2.148	3.5/6	0./18
	residue	0	ПА	residue	5				
	residue	5		residue	5				
114	residue	0	HB2 UC <sup>#</sup>	residue	0	HA IIA	2 (52	E 400	1 000
114	residue	0	п0#	residue	3	пА	5.652	5.482	1.822

115	residue	6	HB2	residue	6	HN	2.332	4.048	0.616
116	residue	6	HN	residue	6	HG#	2.915	4.498	1.332
117	residue	6	HB#	residue	6	HN	2.145	3.570	0.716
118	residue	6	HN	residue	6	HG1	3.434	4.371	2.497
119	residue	6	HN	residue	6	HG2	3.326	4.091	2.561
120	residue	6	HA	residue	6	HN	2.520	3.024	2.016
121	residue	6	HA	residue	6	HG1	3.433	4.420	2.446
122	residue	6	HN	residue	5	HN	3.375	6.050	2.700
123	residue	6	HA	residue	7	HN	2.600	3.470	1.730
124	residue	6	HG#	residue	7	HN	3.432	5.118	1.746
125	residue	6	HB#	residue	7	HN	2.853	4.424	1.282
126	residue	6	HA	residue	8	HN	3.468	4.162	2.774
127	residue	7	HA1	residue	7	HA2	2.031	2.342	1.625
128	residue	7	HA1	residue	7	HN	2.053	2.766	1.342
129	residue	7	HA2	residue	7	HN	2.545	3.254	1.836
130	residue	8	HN	residue	7	HN	2.476	3.971	1.981
131	residue	8	HN	residue	7	HA1	3.181	3.817	2.545
132	residue	8	HN	residue	7	HA2	2.813	3.376	2.250
133	residue	8	HA1	residue	8	HN	2.928	4.214	1.642
134	residue	8	HA2	residue	8	HN	2.103	3.286	0.982

## References

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