Supplementary Material

SOLUTION STRUCTURE OF THE FACTOR H BINDING PROTEIN, A PROTECTIVE ANTIGEN OF *NEISSERIA MENINGITIDIS*

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Fig. S1. 2D ^{15}N-^{1}H HSQC spectrum (900MHz, 298K) of fHbp. The protein concentration was 0.5 mM, in 50 mM phosphate buffer pH 7.

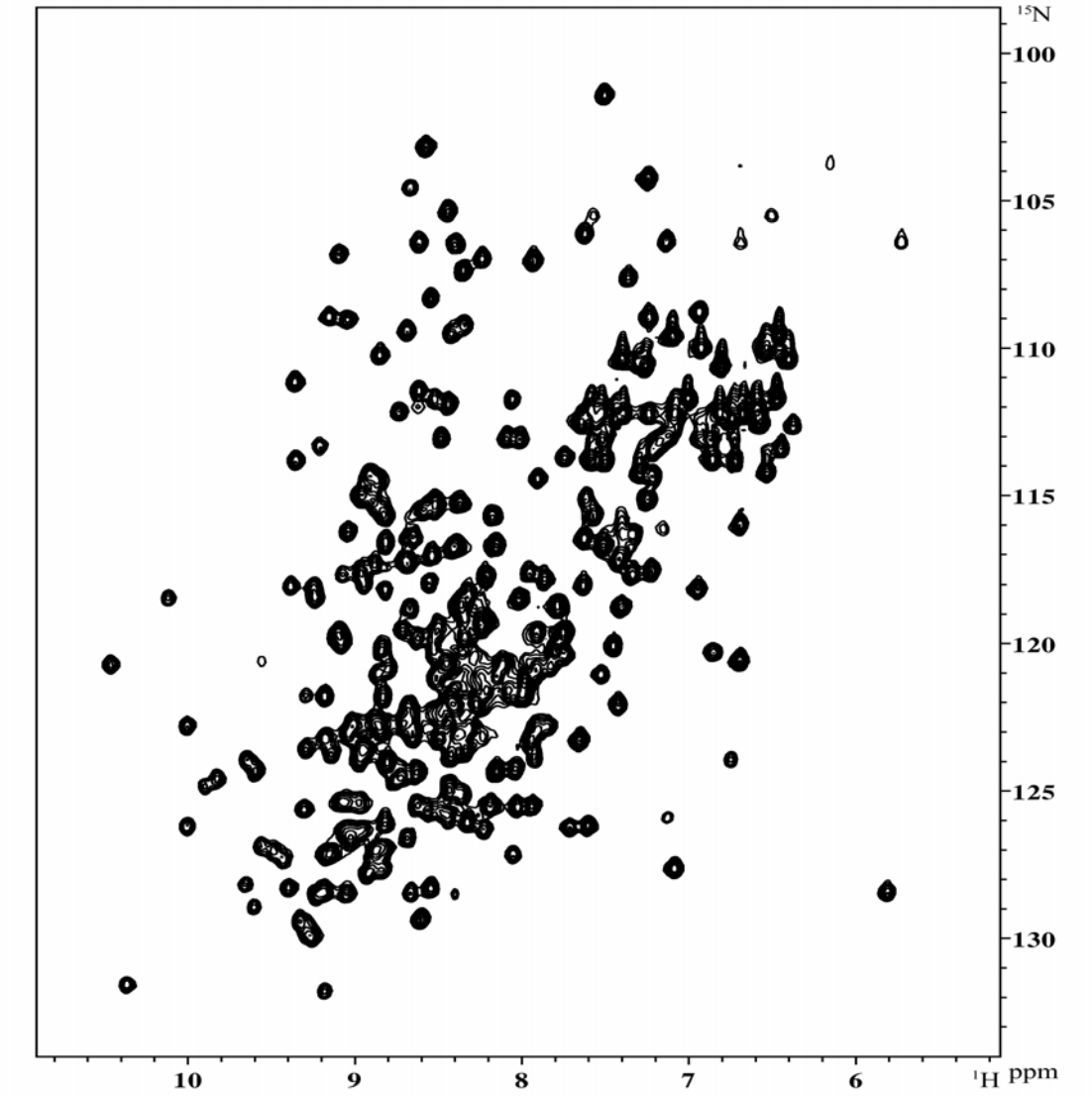

Fig. S2. Solution structures of the fHbp (residues 11-255). The radius of the tube is proportional to the backbone RMSD of each residue. The secondary structure elements are shown: β-strands of the N-terminal domain are shown in cyan and helices in red, while β-strands of the C-terminal domain are in blue. When the residues of the secondary structure elements are superimposed, the backbone RMSD is 1.1 Å.

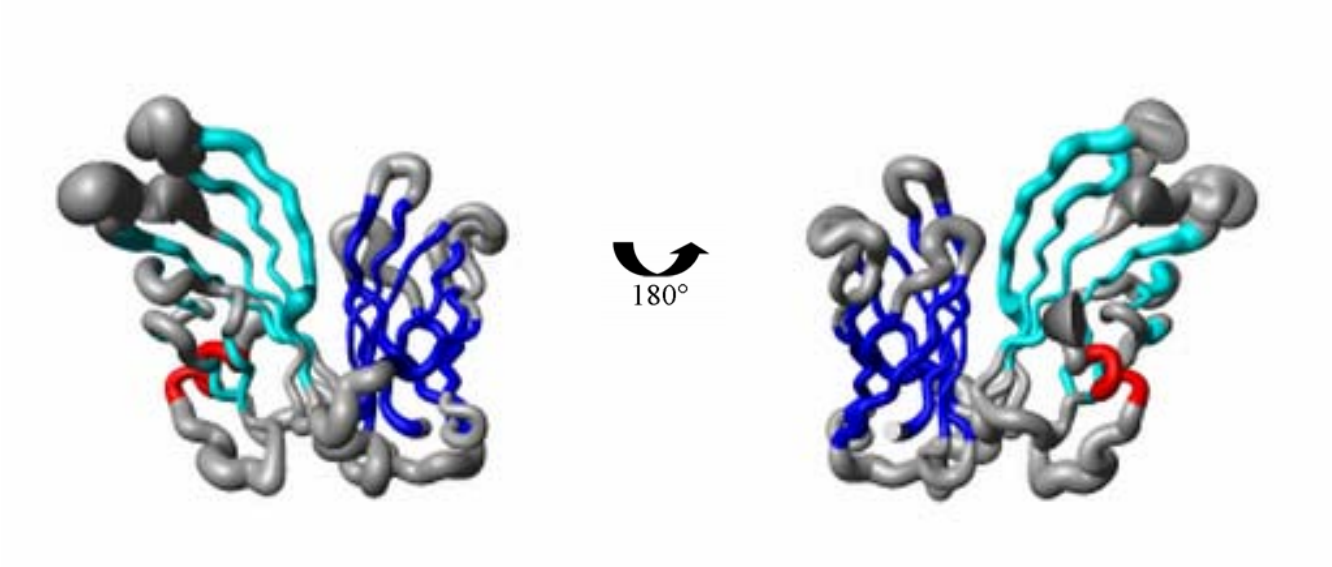

Fig. S3. Experimental ^{15}N R_1, R_2 rates and heteronuclear NOEs of fHbp and spectral density functions $J(\omega_H)$, $J(\omega_N)$, $J(0)$ as obtained from the ^{15}N relaxation data. The experimental data are measured at 500 MHz and 298 K, on a 0.5 mM sample in 50 mM phosphate buffer pH 7.

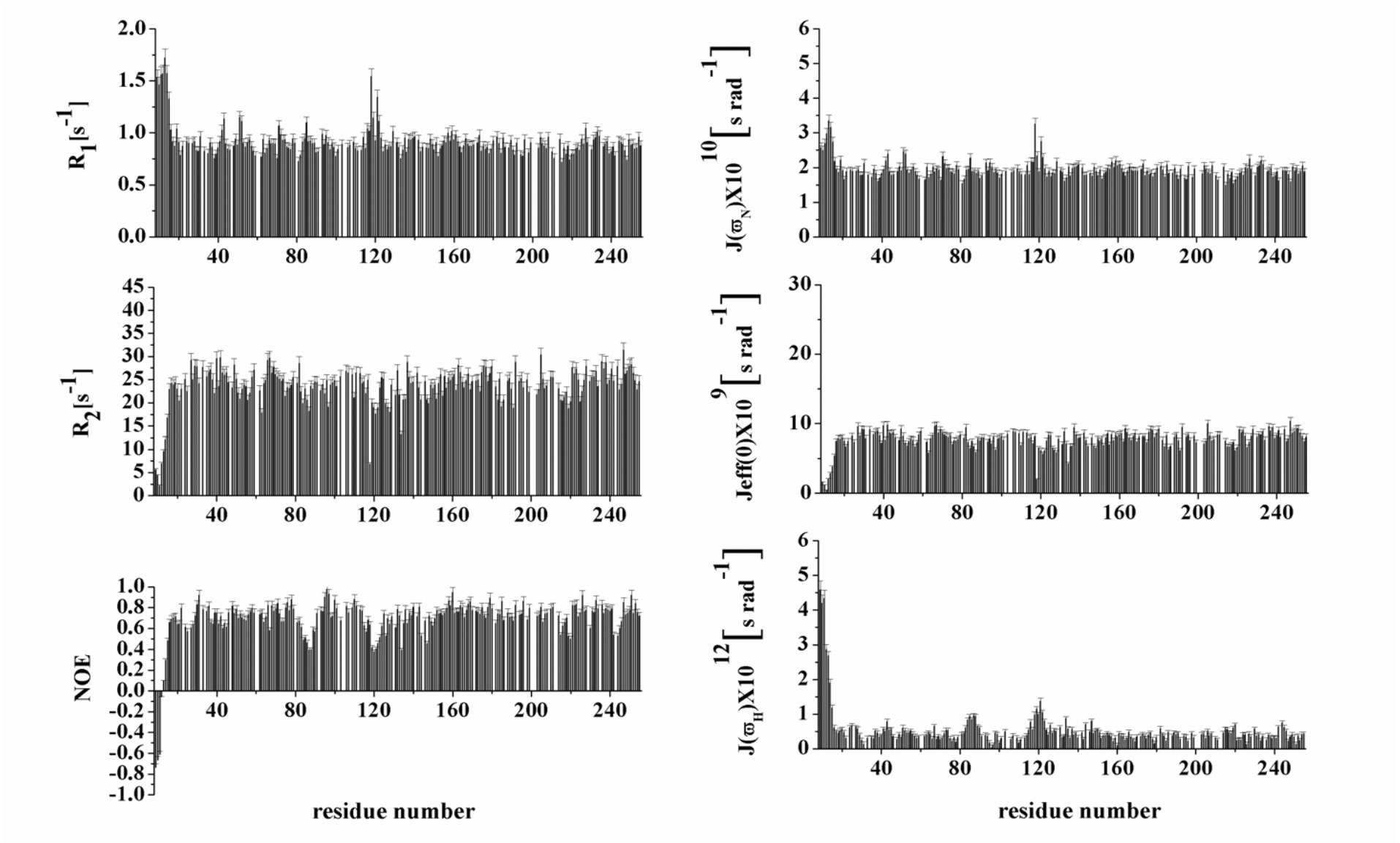

Fig. S4. Number of meaningful NOEs per residue of the fHbp protein. White, light gray, dark gray and black bars indicate intra-residue, sequential, medium-range, and long-range connectivities, respectively.

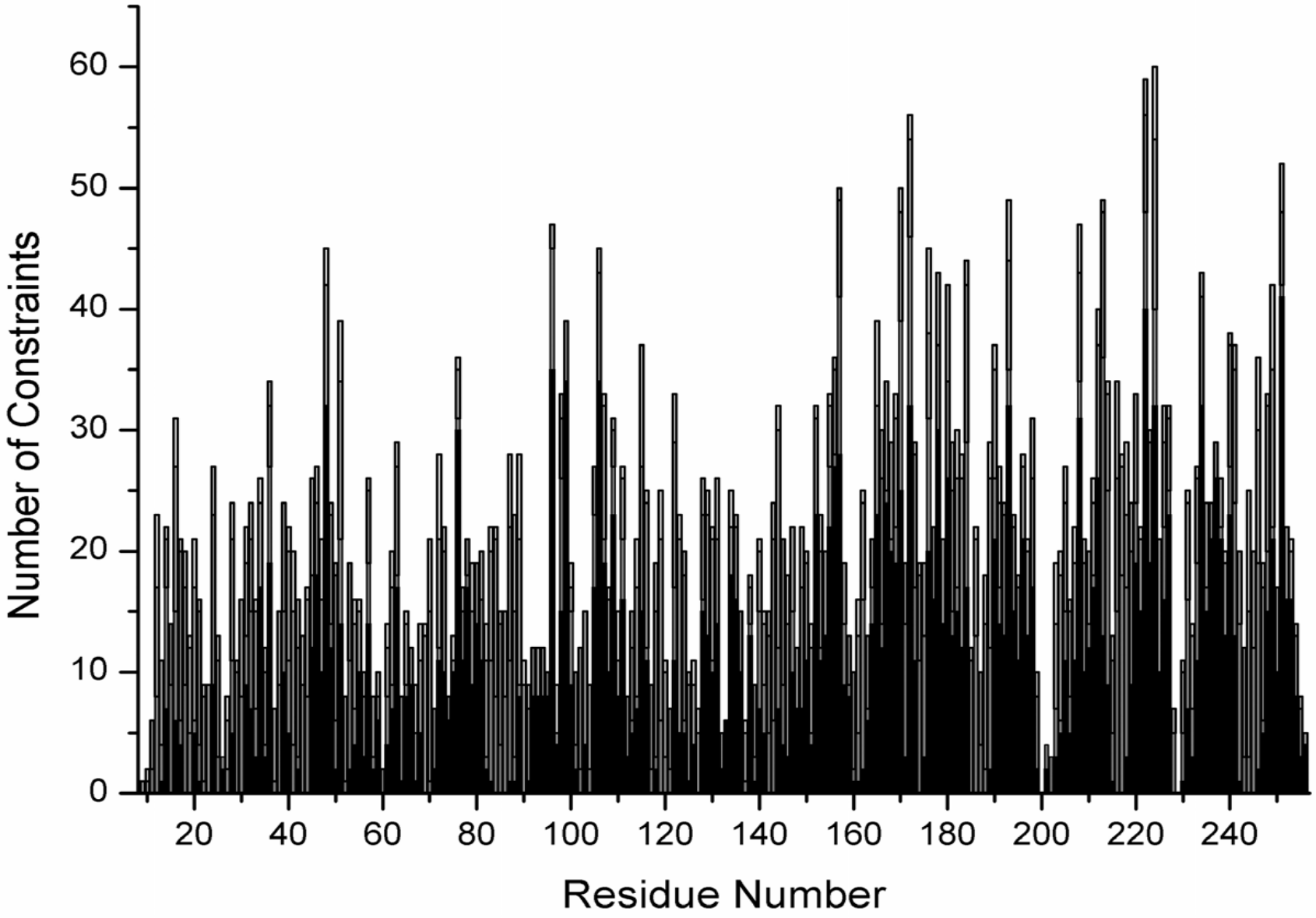

Fig. S5. RMSD values per residue to the mean structure for the backbone (filled squares) and all heavy atoms (open circles) of the family of 30 conformers of fHbp after energy minimization (residues 14-255). The secondary structure elements are also reported at the top.

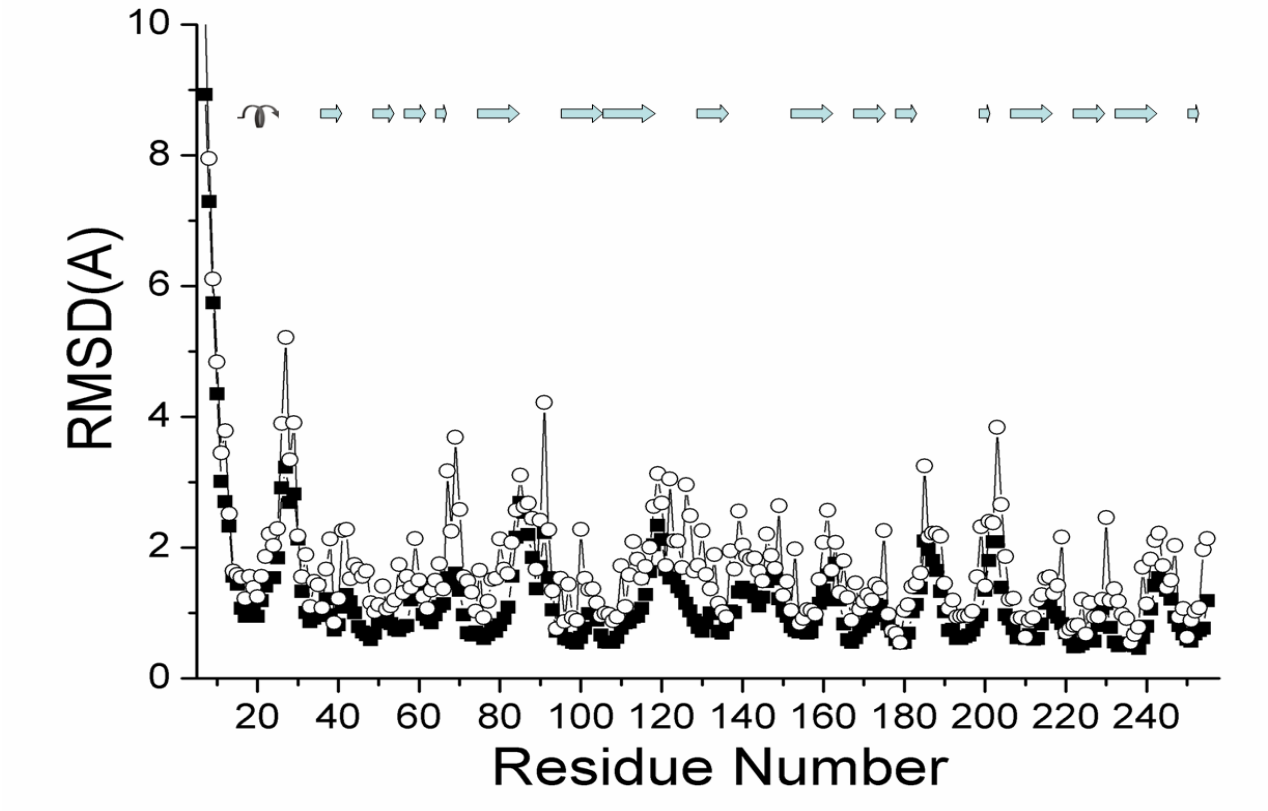

Fig.S6 Combined chemical shift differences ($\Delta\delta^{comb}$) between the isolated fHbp C-terminal domain(9;10), and the same stretch in the full length protein. The $\Delta\delta^{comb}$ are calculated from the experimental ^{1}H and ^{15}N chemical shift variations ($\Delta\delta(^{1}H)$ and $\Delta\delta(^{15}N)$, respectively) measured between corresponding peaks in the two constructs, through the following equation

$$\Delta\delta^{combined} = \sqrt{\frac{\left(\Delta\delta\left(^{1}\mathrm{H}\right)\right)^{2} + \frac{1}{25}\left(\Delta\delta\left(^{15}\mathrm{N}\right)\right)^{2}}{2}}$$

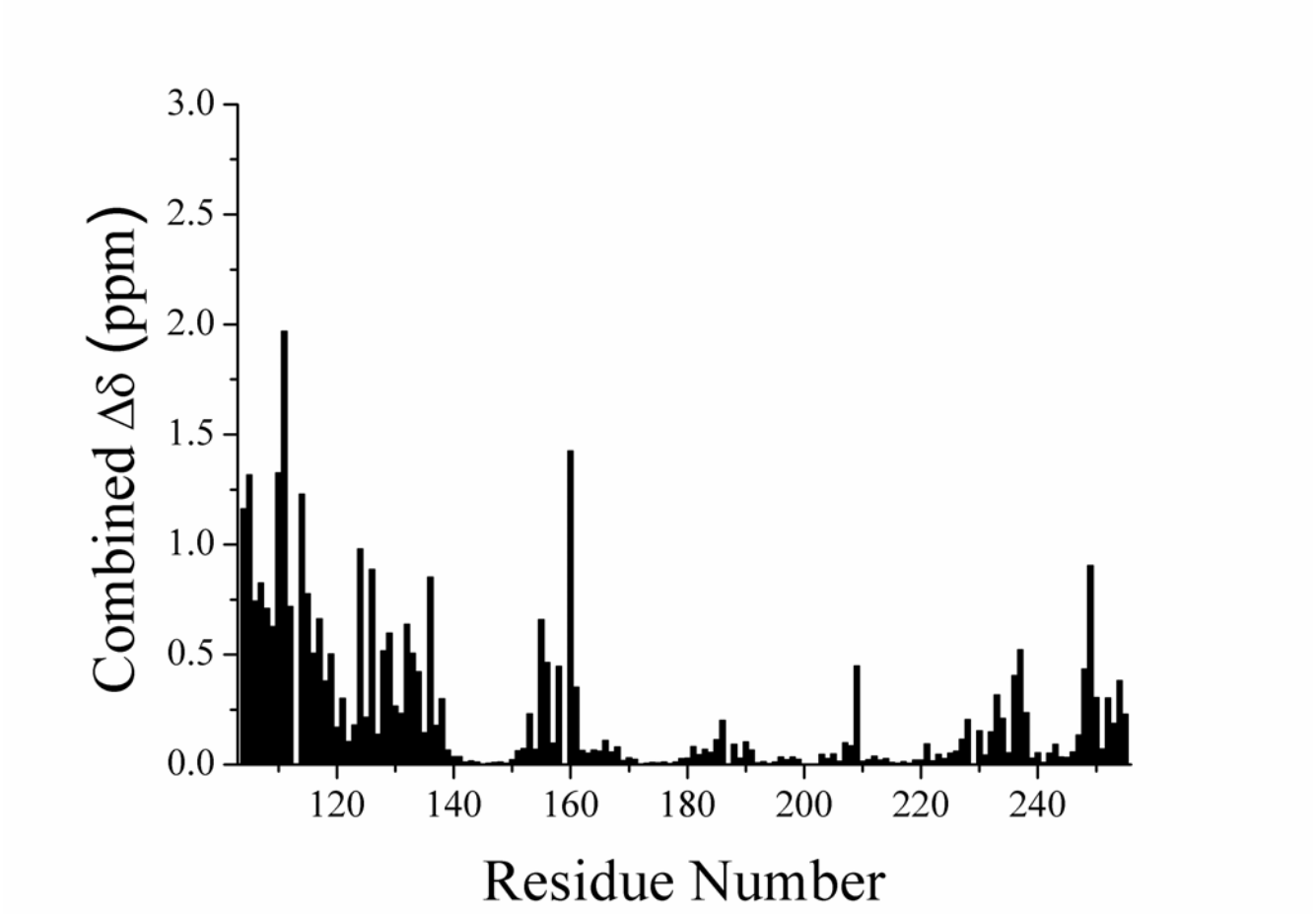

Fig. S7. Observed versus calculated residual dipolar couplings in the final structure refinement with the RDC constraints. The line represents the expected correlation ($y = x$).
The RDC values of the following residues were used for structure calculations: 10-12,21-22,26,39,43-46,48,51,56,59,65,66,68,72,75,87,88,90,94,100,101,104,109,110,118-120,122-123,126,127,129,130,135,136,142,146,147,150,158,165,171-174,177,185,189,201,202,204,207,208,211,212,214-218,228,230-233,243,244,246

Table S1. Acquisition parameters for NMR experiments performed on fHbp.

Experiments [b]	Dimension of acquired data (nucleus)			Spectral width (ppm)			n[a]	Refs
	t_1	t_2	t_3	F_1	F_2	F_3		
[^{1}H-^{1}H]-NOESY [c]	976(^{1}H)	2048(^{1}H)		15	15		120	(11)
^{1}H-^{15}N-HSQC	192(^{15}N)	1024(^{1}H)		40	14		4	(12)
^{1}H-^{13}C-HSQC	256(^{13}C)	2048(^{1}H)		80	14		8	(13)
trhncocacb [d]	112(^{13}C)	54(^{15}N)	1024(^{1}H)	75	41	14	40	(14)
trhncacb [d]	112(^{13}C)	54(^{15}N)	1024(^{1}H)	75	41	14	32	(14)
trhnco [d]	80(^{13}C)	56(^{15}N)	1024(^{1}H)	18	40	16	8	(15)
trhncaco [d]	80(^{13}C)	56(^{15}N)	1024(^{1}H)	18	39	16	16	(16)
trhnca [d]	88(^{13}C)	52(^{15}N)	1024(^{1}H)	14	41	75	16	(14)
trhncoca [d]	88(^{13}C)	52(^{15}N)	1024(^{1}H)	14	41	75	32	(14)
hbhaconh	128(^{1}H)	48(^{15}N)	1024(^{1}H)	14	40	14	24	(17)
(Hb)Cb(CgCd)H	80(^{1}H)	2048(^{13}C)		14	40		224	(18)
(H)CCH-TOCSY [e]	240(^{13}C)	80(^{13}C)	1024(^{1}H)	14	80	80	8	(19)
^{15}N-edited [^{1}H-^{1}H]-NOESY	240(^{1}H)	56(^{15}N)	2048(^{1}H)	15	41	15	8	(20);(13)
^{13}C-edited [^{1}H-^{1}H]-NOESY [e]	192(^{1}H)	64(^{13}C)	2048(^{1}H)	14	80	14	16	(25))
^{13}C-edited [1H-1H]-NOESY [f]	128(^{1}H)	56(^{13}C)	2048(^{1}H)	14	24	14	8	(25)
^{15}N R_1 [g]	256(^{15}N)	1024(^{1}H)		40	14		8	(7;21)
^{15}N R_2 [g]	256(^{15}N)	1024(^{1}H)		40	14		16	(7;21)
^{1}H-^{15}N NOE [g]	480(^{15}N)	1024(^{1}H)		40	14		32	(7;21)

[a] number of acquired scans. [b] All the experiments were acquired on a 500, 700 and 900 MHz spectrometer equipped with a triple resonance cryoprobe at 298 K. All the triple resonance (TXI 5-mm) probes used were equipped with Pulsed Field Gradients along the z-axis. [c] The experiment was acquired in D_2O for the assignment of the aromatic protons. [d] The experiments were acquired on ^{15}N ^{13}C ^{2}H sample. [e] The F2 carrier was at 39 ppm. [f] The F2 carrier was at 43 ppm. [g] The ^{15}N longitudinal relaxation rates, R_1, were measured using delays in the pulse sequence of 2.5, 35, 75, 125, 200, 370, 500, 675, 1000, 2000, and 3000 ms for all samples. The ^{15}N transverse relaxation rates, R_2, were measured using the CPMG sequence. The relaxation delays used were 16.96, 33.92, 50.88, 84.81, 118.72, 152.64, 169.60, 220.48, 254.40, 305.28 ms. The interscan delay (d1) was 3 s for R_1 and R_2 and 6 s for ^{1}H-^{15}N NOE respectively. All 3D and 2D spectra were processed using the standard Bruker software TOPSPIN and analyzed through CARA and XEASY programs (22-24)

Table S2 ^{1}H, ^{15}N and ^{13}C resonance assignments for fHpb at 298 K, pH 7.0, in water solution. In total, the resonances of 80% of carbon atoms, 97% of nitrogen atoms and 99% of protons were assigned. Proton resonances were calibrated with respect to the signal of 2,2-dimethylsilapentane-5-sulfonic acid (DSS). Nitrogen chemical shifts were referenced indirectly to the ^{1}H standard using a conversion factor derived from the ratio of NMR frequencies. Carbon resonances were calibrated using the signal of dioxane at 69.4 ppm (298 K) as secondary reference.

aa	N (HN)	CO	Cα (Hα)	Cβ (Hβ)	Others
ALA -9	128.5 (8.40)	177.3	52.2 (4.22)	19.3 (1.30)	
ALA-10	123.7 (8.34)	177.2	51.8 (4.15)	19.3 (1.26)	
ASP-11	119.2 (8.23)	176.4	53.7 (4.49)	40.6 (2.60 , 2.49)	
ILE-12	121.3 (7.99)	176.9	61.8 (4.01)	38.1 (1.84)	Cδ1 12.9 (0.76) Cγ1 26.8 (1.10 , 1.35) Cγ2 17.4 (0.80)
GLY-13	111.8 (8.44)	173.7	44.9 (3.81)		
ALA-14	123.2 (7.95)	178.0	52.4 (4.21)	19.3 (1.30)	
GLY-15	107.4 (8.35)	174.3	45.6 (4.02 , 3.77)		
LEU-16	117.6 (7.22)	178.2	57.9 (3.74)	40.7 (1.37 , 0.99)	Cδ1 24.9 (0.66) Cδ2 21.7 (0.18) Cγ 24.4 (1.28)
ALA-17	117.8 (7.86)	181.1	54.9 (3.94)	17.2 (1.38)	
ASP-18	118.4 (8.02)	177.9	56.3 (4.22)	39.3 (2.25 , 2.56)	
ALA-19	121.5 (8.21)	178.9	55.0 (3.95)	17.8 (1.42)	
LEU-20	113.4 (7.22)	177.5	55.5 (4.26)	42.2 (1.95 , 1.29)	Cδ1 23.3 (0.65) Cγ 26.0 (0.84)
THR-21	106.1 (7.62)	175.0	61.7 (4.39)	71.5 (4.14)	Cγ2 20.9 (1.15)
ALA-22	127.8 (8.93)	176.0	50.7 (4.62 , 6.50)	18.7 (1.34)	
PRO-23			61.5 (4.43)	31.8 (2.19 , 1.85)	Cδ 50.1 (3.75 , 3.55) Cγ 26.5 (1.92 , 1.83)
LEU-24	121.0 (8.15)	176.4	55.5 (3.89)	40.9 (1.47 , 1.22)	Cδ1 16.2 (0.63) Cδ2 25.1 (0.72) Cγ 26.7 (1.37)
ASP-25	124.7 (8.76)	176.4	52.7 (4.63)	42.8 (2.24 , 2.77)	
HIS-26			58.1 (4.27)	29.2 (3.08)	Hδ2 6.92 Hε1 7.71
LYS-27	118.4 (8.35)	177.4	56.3 (3.97)	30.9 (1.58)	Cε 40.9 (2.85) Cγ 23.7 (1.07 , 0.97) Cδ 27.9 (1.51)
ASP-28	120.0 (7.45)	176.2	54.2 (4.31)	40.1 (2.56 , 2.44)	
LYS-29	121.9 (8.42)	177.4	56.3 (3.96)	31.9 (1.64)	Cδ 33.1 (1.56) Cγ 24.8 (1.42 , 1.28) Cε 42.1 (2.54)
GLY-30	111.5 (8.61)	174.2	44.8 (3.56 , 3.52)		
LEU-31	127.2 (8.05)	177.9	55.9 (3.77)	44.4 (1.23 , 0.76)	Cδ1 26.9 (0.39) Cδ2 22.7 (0.71) Cγ 27.3 (1.54)
GLN-32	131.8 (9.18)	174.3	57.9 (3.44)	27.7 (2.02 , 1.95)	Cγ 34.6 (2.19 , 2.05) Nε2 112.5 (7.57 , 6.57)
SER-33	108.9 (7.24)	171.1	56.8 (4.98)	64.6 (3.64 , 3.44)	
LEU-34	121.8 (8.01)	174.7	53.3 (4.37)	45.6 (1.15)	Cδ1 26.2 (0.37) Cγ 26.4 (1.24) Cδ2 26.2 (0.46)
THR-35	123.9 (8.81)	172.8	62.6 (4.05)	68.2 (3.85)	Cγ2 22.0 (0.93)
LEU-36	128.4 (8.66)	174.7	53.8 (4.15)	40.6 (1.87 , 0.81)	Cδ1 22.1 (0.47) Cδ2 25.5 (0.10) Cγ 25.0 (1.47)
ASP-37	123.2 (8.50)		54.7 (4.84)	43.1 (2.70 , 2.44)	
GLN-38	120.7 (10.45)	178.5	56.3 (3.81)	28.2 (1.89 , 1.42)	Cγ 33.7 (2.37 , 2.27) Nε2 113.8 (7.50 , 6.72)
SER-39	111.7 (8.52)	171.8	61.4 (4.08)	63.0 (3.79 , 3.56)	
VAL-40	116.0 (6.69)	172.3	60.4 (3.89)	32.3 (1.77)	Cγ1 21.3 (0.77) Cγ2 18.9 (0.59)
ARG-41	125.4 (8.18)	176.9	55.6 (4.18)	30.6 (2.15 , 1.67)	Cδ 42.4 (2.98) Cγ 27.1 (1.30 , 1.50)
LYS-42	119.4 (8.49)	176.6	58.7 (3.78)	32.0 (1.64 , 1.48)	Cε 41.8 (2.84) Cγ 24.7 (1.43) Cδ 28.6 (1.52)
ASN-43	115.5 (8.51)	173.9	55.1 (4.44)	37.1 (3.12 , 2.82)	Nδ2 113.1 (7.52 , 6.88)

GLU-44	118.7 (7.79)	175.3	54.8 (4.77)	32.3 (2.19 , 1.78)	
LYS-45	117.1 (8.71)	174.3	52.8 (4.61)	35.2 (1.43)	Cδ 28.3 (1.52) Cε 42.3 (2.82) Cγ 24.0 (1.24 , 1.20)
LEU-46	125.3 (9.09)	173.8	52.6 (5.04)	44.9 (1.74 , 1.03)	Cδ1 24.7 (0.09) Cγ 25.3 (1.19)
LYS-47	129.8 (9.26)	175.6	53.9 (5.05)	33.0 (1.72 , 1.52)	Cδ 30.4 (1.59) Cε 41.1 (2.63) Cγ 28.1 (1.53)
LEU-48	126.3 (8.95)	175.6	52.0 (5.46)	44.4 (0.89 , 0.84)	Cδ1 24.2 (-0.32) Cδ2 23.1 (0.10) Cγ 26.6 (0.67)
ALA-49	120.8 (8.80)	176.3	51.0 (5.30)	23.5 (1.36)	
ALA-50	120.7 (8.12)	176.3	53.0 (4.49)	23.7 (1.39)	
GLN-51	116.3 (9.04)	175.3	56.1 (3.77)	27.3 (2.25 , 1.89)	Cγ 34.0 (2.35 , 2.31) Nε2 112.0 (7.53 , 6.82)
GLY-52	105.4 (8.44)	173.1	45.0 (4.07 , 3.51)		
ALA-53	124.4 (8.15)	176.0	49.9 (4.77)	22.7 (1.41)	
GLU-54	116.7 (8.16)	174.2	54.3 (5.49)	34.3 (1.91 , 1.75)	Cγ 32.9 (2.03)
LYS-55	122.9 (8.85)	172.9	56.4 (4.19)	34.7 (1.92 , 1.73)	Cδ 29.2 (1.42) Cγ 23.9 (1.18)
THR-56	120.8 (7.91)	173.1	62.0 (4.91)	68.6 (3.69)	Cγ2 21.9 (0.94)
TYR-57	127.4 (9.43)	174.2	57.4 (4.49)	41.9 (2.75 , 2.54)	Qδ 6.79 Qε 6.44
GLY-58	108.9 (9.15)	172.5	42.3 (3.54)		
ASN-59	117.3 (8.88)	176.3	57.1 (4.03)	39.7 (2.64 , 2.19)	
GLY-60	114.9 (8.95)	174.1	44.9 (4.22 , 3.35)		
ASP-61	122.0 (7.99)	174.7	54.4 (4.49)	41.8 (3.15 , 2.87)	
SER-62	113.1 (8.48)	173.1	57.2 (4.96)	64.5 (3.61 , 3.50)	
LEU-63	126.4 (9.00)	175.9	53.1 (4.50)	43.8 (1.58 , 1.04)	Cδ1 22.2 (0.29) Cγ 25.9 (0.40)
ASN-64	125.6 (8.48)	173.9	50.6 (4.75)	35.2 (3.72 , 2.60)	
THR-65	113.8 (7.75)	177.2	63.2 (4.77)	63.5 (3.85)	Cγ2 23.5 (0.75)
GLY-66	114.4 (8.87)	173.3	44.9 (3.84 , 3.72)		
LYS-67	112.6 (6.38)	176.3	54.3 (4.02)	32.2 (1.45)	Cε 42.0 (2.62) Cγ 27.8 (1.35)
LEU-68	116.7 (7.33)	176.3	52.5 (4.28)	40.6 (1.38)	Cδ1 22.4 (0.72) Cγ 30.2 (1.29)
LYS-69	119.8 (8.51)	175.9	55.0 (3.99)	32.4 (1.47)	Cδ 28.2 (1.48) Cε 41.9 (2.87 , 2.81) Cγ 24.5 (1.29 , 1.19)
ASN-70	121.5 (8.08)	174.4	54.4 (3.84)	38.1 (2.41 , 2.16)	Nδ2 112.3 (7.46 , 6.74)
ASP-71	113.4 (9.22)	173.0	54.7 (3.69)	38.5 (2.75 , 2.86)	
LYS-72	113.4 (6.44)	174.7	53.1 (4.41)	36.1 (1.50 , 1.23)	Cε 39.3 (2.79) Cγ 23.4 (1.11 , 1.04)
VAL-73	122.1 (8.68)	176.6	62.1 (4.19)	32.0 (1.71)	Cγ1 21.2 (0.39)
SER-74	127.0 (9.50)	172.2	58.3 (4.51)	64.0 (3.31)	
ARG-75	122.6 (7.85)	173.3	55.3 (5.03)	31.9 (1.64)	Cδ 41.8 (2.82) Cγ 28.8 (1.32)
PHE-76	118.1 (9.25)	175.8	55.2 (4.81)	43.6 (2.94)	Qδ 7.09 Qε 6.98
ASP-77	123.6 (9.14)	176.5	55.1 (5.36)	41.3 (2.81 , 2.69)	
PHE-78	119.7 (9.09)	174.0	54.9 (6.43)	42.5 (2.62 , 2.96)	Qδ 6.11 Qε 6.44 HZ 6.42
ILE-79	119.8 (8.62)	174.0	61.2 (4.33)	41.9 (1.59)	Cδ1 13.2 (0.70) Cγ1 27.5 (1.48 , 0.92) Cγ2 18.0 (0.84)
ARG-80	128.4 (9.05)	174.9	54.4 (5.31)	33.7 (1.70)	Cγ 33.0 (1.54) Cδ 41.8 (1.13)
GLN-81	125.5 (9.30)	173.7	53.7 (5.56)	34.0 (1.75)	Cγ 34.1 (1.96) Nε2 109.9 (6.93 , 6.55)
ILE-82	115.5 (8.59)	172.5	59.6 (4.58)	42.2 (1.65)	Cδ1 13.5 (0.74) Cγ1 26.7 (1.35 , 0.93) Cγ2 16.8 (0.82)
GLU-83	124.9 (8.43)	175.6	54.8 (4.94)	30.5 (1.79 , 1.58)	Cγ 35.8 (1.58 , 1.72)
VAL-84	127.0 (8.88)	175.7	61.4 (4.08)	34.0 (1.76)	Cγ1 20.5 (0.74)
ASP-85	129.4 (9.33)	175.8	55.1 (4.16)	38.9 (2.83 , 2.46)	
GLY-86	103.3 (8.57)	173.4	44.8 (3.99 , 3.51)		
GLN-87	119.7 (7.75)	173.9	53.3 (4.48)	30.7 (1.95 , 1.83)	Cγ 32.9 (2.20 , 2.15)

LEU-88	123.5 (8.42)	176.3	53.8 (4.63)	41.7 (1.47 , 1.12)	Cδ1 24.1 (0.65) Cδ2 23.0 (0.53) Cγ 26.7 (1.35)
ILE-89	127.2 (9.15)	175.7	59.4 (4.25)	39.6 (1.76)	Cδ1 11.7 (0.63) Cγ1 26.9 (1.26 , 1.12) Cγ2 16.8 (0.68)
THR-90	123.1 (8.66)	172.9	62.6 (4.20)	68.6 (4.03)	Cγ2 21.6 (1.03)
LEU-91	125.3 (8.97)	177.4	55.5 (4.26)	44.3 (1.42 , 1.30)	Cδ1 25.4 (0.67)
GLU-92	116.7 (7.50)	172.7	54.7 (5.03)	33.7 (2.12 , 1.96)	Cγ 36.2 (2.41, 2.50)
SER-93	117.9 (8.95)	172.8	57.3 (4.25)	65.5 (3.89 , 3.44)	
GLY-94	108.6 (6.93)	171.1	46.6 (3.69)		
GLU-95	128.2 (9.67)	173.2	54.8 (5.64)	34.3 (2.36 , 2.30)	Cγ 39.2 (2.15)
PHE-96	131.6 (10.37)	173.0	54.6 (5.05)	42.1 (2.82 , 2.6)	Qδ 7.04 Qε 6.11
GLN-97	126.5 (8.69)	174.2	53.2 (4.96)	28.8 (1.97)	Cγ 32.9 (1.52) Nε2 109.5 (6.44 , 7.10)
VAL-98	118.8 (8.68)	173.8	59.7 (4.57)	35.1 (1.57)	Cγ1 21.5 (0.41) Cγ2 20.0 (0.47)
TYR-99	127.6 (8.90)	173.3	56.9 (4.94)	40.8 (2.77)	Qδ 6.31 Qε 6.11
LYS-100	128.3 (5.81)		55.7 (4.25)	35.9 (1.48)	Cδ 28.4 Cγ 27.9
GLN-101	125.8 (8.44)	174.1	55.1 (5.03)	27.6 (2.27)	Cγ 36.22 (2.13)
SER-102	117.7 (9.06)		63.0 (3.05)	63.2 (3.68)	
HIS-103	118.4 (10.12)		53.8 (4.41)	30.3 (2.23)	Hδ2 6.52 Hε1 7.73
SER-104	112.3 (7.24)		56.7 (4.41)	65.5 (2.82)	
ALA-105	116.8 (8.42)	173.2	51.4 (4.75)	22.3 (1.08)	
LEU-106	115.2 (8.38)	175.3	53.8 (5.55)	46.4 (1.71)	Cδ1 26.8 (1.00) Cδ2 27.4 (0.93) Cγ 28.0 (1.73)
THR-107	109.4 (8.69)	172.5	57.1 (5.29)	71.3 (3.39)	Cγ2 22.8 (0.72)
ALA-108	120.7 (8.46)	173.4	51.0 (4.37)	23.4 (0.95)	
PHE-109	115.0 (8.51)	174.2	56.6 (4.71)	41.9 (2.45)	Qδ 6.05 Qε 6.53 HZ 7.44
GLN-110	124.5 (9.83)	175.2	53.2 (5.23)	29.2 (2.27)	Cγ 35.5 (2.50) Nε2 116.0 (7.42 , 7.16)
THR-111	126.8 (9.57)	174.5	66.4 (4.19)	69.4 (4.04)	Cγ 2 22.7 (1.50)
GLU-112	121.7 (9.30)	177.4	56.2 (4.81)	31.3 (2.12)	Cγ 42.6 (2.44)
GLN-113	117.6 (7.95)	174.0	53.8 (5.23)	32.5 (2.03 , 1.97)	Cγ 33.4 (2.19)
ILE-114	115.0 (8.97)	174.1	59.0 (4.91)	42.8 (1.84)	Cδ1 13.3 (0.76) Cγ1 26.6 (1.41) Cγ2 19.1 (0.89)
GLN-115	122.0 (7.42)	175.7	56.1 (4.41)	28.5 (2.14 , 1.97)	Cγ 33.1 (2.39 , 2.23) Nε2 110.4 (7.40 , 6.41)
ASP-116	125.6 (8.57)	176.7	53.5 (4.38)	41.2 (2.31 , 3.02)	
SER-117	120.7 (8.45)	174.8	60.8 (4.02)	62.6 (3.84)	
GLU-118	119.4 (8.25)	175.9	56.0 (4.04)	29.9 (1.65)	Cγ 35.6 (2.04 , 1.88)
HIS-119	117.3 (7.42)	173.5	54.5 (4.61)	28.7 (2.98 , 2.91)	Hδ2 7.15 Hε1 7.70
SER-120	116.8 (8.40)	175.7	59.1 (4.18)	62.8 (3.78)	
GLY-121	112.2 (8.73)	173.5	44.7 (4.05 , 3.72)		
LYS-122	120.2 (7.80)	175.1	55.1 (4.46)	33.9 (1.81 , 1.76)	Cδ 27.7 (1.48 , 1.31) Cγ 24.6 (1.25 , 1.20)
MET-123	119.8 (8.35)	176.2	52.9 (5.08)	33.8 (1.76 , 1.82)	Cγ 30.6 (2.45 , 2.24) Cε1 16.2 (1.47)
VAL-124	118.5 (9.24)	174.0	59.1 (4.47)	34.4 (1.97)	Cγ1 19.5 (0.77)
ALA-125	125.9 (8.33)	177.2	52.0 (4.62)	18.2 (1.27)	
LYS-126	126.1 (7.60)	172.6	56.0 (4.05)	34.5 (1.48)	Cδ 30.6 (1.99) Cγ 28.9 (1.55) Cε 41.7 (2.84)
ARG-127	122.8 (8.31)	176.3	55.6 (4.90)	28.3 (1.52)	Cγ 27.9 (1.64)
GLN-128	121.0 (7.53)	172.2	54.2 (4.54)	32.1 (2.02 , 1.87)	Cγ 33.7 (2.18) Nε2 110.5 (7.26 , 6.81)
PHE-129	125.5 (8.62)	174.5	56.0 (6.04)	42.1 (3.14 , 2.99)	Qδ 7.09 Qε 6.75
ARG-130	125.3 (8.02)	172.1	53.4 (4.37)	32.3 (1.45)	Cδ 42.0 (2.76) Cγ 27.0 (1.50)
ILE-131	121.9 (8.46)	175.5	58.3 (3.88)	35.7 (1.84)	Cδ1 8.5 (0.38) Cγ1 27.0 (1.12) Cγ2 17.5 (0.79)
GLY-132	115.7 (8.81)	171.6	44.2 (4.06)		
ASP-133	123.7 (7.91)	174.1	54.8 (4.58)	45.4 (2.35 , 2.11)	

ILE-134	119.1 (8.26)	174.8	61.6 (4.39)	37.5 (1.83)	Cδ1 14.1 (0.78) Cγ1 26.6 (0.94) Cγ2 17.9 (0.73)
ALA-135	129.3 (8.61)	173.4	50.6 (4.76)	23.3 (1.39)	
GLY-136	101.2 (7.51)	172.6	44.3 (3.55 , 4.42)		
GLU-137	121.0 (8.22)	174.9	53.1	28.3 (2.13 , 2.04)	Cγ 34.3 (2.21)
HIS-138	124.2 (8.05)	175.4	57.9 (4.77)	27.7 (3.43)	Hδ2 7.09 Hε1 8.15
THR-139	125.3 (9.06)	174.2	63.2 (3.86)	68.1 (3.19)	Cγ2 22.1 (1.04)
SER-140	121.8 (8.83)	176.7	58.0 (4.56)	63.0 (4.00 , 3.64)	
PHE-141	128.8 (9.60)	175.4	61.3 (3.95)	39.4 (2.60 , 2.51)	Qδ 6.81 Qε 7.13
ASP-142	113.1 (8.02)	175.4	55.2 (4.35)	41.0 (2.83 , 2.35)	
LYS-143	117.7 (7.34)	175.6	54.1 (4.44)	32.5 (2.07 , 1.46)	Cδ 30.2 (1.83 , 1.59) Cε 42.6 (2.83) Cγ 24.6 (1.28 , 1.17)
LEU-144	120.5 (6.70)	174.1	52.8 (3.90)	41.0 (1.12 , 1.25)	Cδ1 26.3 (0.62) Cδ2 22.1 (0.72) Cγ 25.7 (1.82)
PRO-145		172.7	62.7 (4.04)	30.1 (1.90 , 0.93)	Cδ 49.6 (3.18 , 2.27) Cγ 26.8 (0.67 , 1.35)
GLU-146	119.1 (8.34)	176.0	56.1 (3.97)	30.1 (1.94 , 1.74)	Cγ 35.9 (2.14 , 2.10)
GLY-147	104.3 (7.24)	171.7	43.9 (3.92 , 3.81)		
GLY-148	107.0 (8.24)	171.8	43.6 (3.71 , 4.35)		
ARG-149	117.8 (8.21)	175.0	54.2 (5.38)	33.0 (1.55)	Cδ 42.4 (2.99) Cγ 26.8 (1.41 , 1.30)
ALA-150	126.6 (9.03)	175.0	50.7 (4.73)	23.4 (1.22)	
THR-151	117.9 (8.56)	171.9	62.0 (4.85)	69.7 (3.76)	Cγ2 21.2 (1.03)
TYR-152	126.1 (10.01)	174.6	55.8 (4.58)	40.1 (2.72 , 2.40)	Qδ 6.90 Qε 6.54
ARG-153	121.0 (8.86)	177.4	54.0 (5.40)	33.5 (1.90 , 1.73)	Cδ 42.6 (3.13) Cγ 27.9 (1.63)
GLY-154	114.2 (8.92)	173.8	46.8 (4.82 , 4.42)		
THR-155	126.4 (9.06)	170.4	62.3 (4.71)	72.6 (3.18)	Cγ2 21.1 (0.86)
ALA-156	127.5 (7.09)	174.0	48.8 (5.29)	22.6 (0.82)	
PHE-157	117.0 (8.54)	171.9	53.3 (5.44)	41.0 (3.23 , 2.48)	Qδ 6.86 Qε 6.69
GLY-158	108.4 (8.55)	173.1	42.6 (3.12 , 4.0)		
SER-159	115.2 (7.61)	176.1	58.8 (3.42)	61.9 (3.57)	
ASP-160	124.8 (9.89)	175.2	55.4 (4.17)	39.2 (2.86 , 2.70)	
ASP-161	116.7 (7.52)	172.7	54.3 (4.57)	40.6 (2.49 , 2.29)	
ALA-162	128.2 (8.54)	177.7	49.9 (4.92)	17.5 (1.25)	
GLY-163	106.5 (8.41)	174.3	45.0 (4.29 , 3.89)		
GLY-164	106.4 (7.13)	173.9	45.2 (4.12 , 3.64)		
LYS-165	123.9 (9.65)	174.4	53.5 (5.05)	34.6 (1.69)	Cδ 29.1 (1.56) Cγ 23.7 (1.45 , 1.29)
LEU-166	126.3 (7.71)	174.8	52.7 (4.87)	44.6 (1.06)	Cδ1 25.3 (0.72) Cδ2 23.8 (0.60) Cγ 26.8 (0.33)
THR-167	123.0 (8.37)	172.1	61.8 (4.95)	70.2 (3.78)	Cγ2 20.3 (1.06)
TYR-168	128.1 (9.17)	172.2	58.2 (4.77)	43.7 (2.41 , 2.21)	Qδ 6.57 Qε 7.26
THR-169	124.5 (8.71)	172.5	60.8 (5.40)	70.8 (3.59)	Cγ2 20.4 (0.89)
ILE-170	123.7 (8.93)	173.1	60.6 (4.31)	41.3 (1.21)	Cδ1 11.8 (0.55) Cγ1 27.1 (0.62) Cγ2 16.2 (-0.33)
ASP-171	125.2 (8.37)	177.2	51.7 (4.75)	41.7 (2.80 , 2.31)	
PHE-172	123.6 (8.97)	176.9	61.5 (3.88)	37.4 (2.99 , 2.38)	Qδ 6.95 Qε 7.06 HZ 7.32
ALA-173	122.1 (8.27)	178.9	54.5 (4.32)	17.6 (1.53)	
ALA-174	118.8 (7.41)	176.6	51.2 (4.10)	18.3 (1.14)	

LYS-175	114.4 (7.91)	174.6	57.0 (3.39)	30.1 (2.20 , 1.90)	Cδ 29.5 (1.61) Cγ 25.8 (1.50)
GLN-176	116.4 (7.63)	174.3	54.4 (5.41)	34.8 (1.73 , 1.66)	Cγ 34.2 (2.18) Nε2 111.9 (7.59 , 6.60)
GLY-177	110.2 (8.85)	170.8	44.6 (5.21 , 3.53)		
ASN-178	112.7 (7.64)	171.5	53.7 (4.22)	41.5 (2.71 , 2.50)	Nδ2 114.1 (7.30 , 6.54)
GLY-179	106.7 (9.10)	172.4	47.2 (4.49 , 4.08)		
LYS-180	121.8 (9.18)	172.5	56.6 (4.82)	35.4 (1.81 , 1.60)	Cδ 28.5 (1.37) Cε 41.6 (2.71) Cγ 23.5 (1.16 , 0.89)
ILE-181	123.4 (8.35)	174.0	60.5 (4.58)	39.6 (1.69)	Cδ1 14.8 (0.56) Cγ2 17.9 (0.73)
GLU-182	122.3 (8.49)	175.4	53.4 (4.47)	35.5 (1.35)	Cγ 37.1 (1.89 , 1.68)
HIS-183	109.6 (8.43)	176.0	57.5 (3.98)	27.4 (3.42 , 3.34)	Hδ2 6.71 Hε1 7.76
LEU-184	124.4 (9.60)	178.8	56.0 (4.28)	39.9 (1.57 , 1.12)	Cδ1 28.3 (0.48) Cδ2 22.4 (0.53) Cγ 31.3 (1.23)
LYS-185	122.9 (10.00)	177.7	57.7 (3.68)	31.9 (1.65 , 1.58)	Cδ 29.0 (1.58 , 1.50) Cγ 24.8 (1.55 , 1.39) Cε 42.0 (2.90)
SER-186	115.2 (7.26)	173.1	54.6 (4.67)	62.7 (3.64 , 3.56)	
PRO-187			65.4 (3.96)	32.1 (2.31 , 1.87)	Cδ 50.7 (3.76 , 4.10) Cγ 27.2 (1.92 , 1.99)
GLU-188	113.0 (8.08)	173.9	56.6 (3.01)	29.6 (1.66 , 1.38)	Cγ 36.6 (1.98 , 1.75)
LEU-189	112.9 (7.13)	175.6	53.8 (3.97)	41.2 (1.39)	Cδ1 20.7 (0.33) Cδ2 24.7 (0.72) Cγ 26.3 (1.24)
ASN-190	117.9 (6.95)	175.7	53.2 (4.60)	36.5 (2.74 , 2.67)	Nδ2 112.4 (7.08)
VAL-191	113.3 (7.18)	174.9	59.8 (4.48)	33.0 (2.16)	Cγ1 21.9 (0.64) Cγ2 17.3 (0.44)
ASP-192	118.1 (8.83)	174.9	54.1 (4.78)	41.6 (2.41)	
LEU-193	123.1 (8.38)	171.1	52.3 (4.15)	38.2 (0.95 , -0.06)	Cδ1 25.4 (0.20) Cδ2 22.6 (-0.03)
ALA-194	126.3 (8.22)	176.2	52.5 (4.10)	20.0 (1.40)	
ALA-195	122.0 (8.28)	178.1	51.8 (4.86)	17.4 (1.10)	
ALA-196	126.0 (8.82)	175.1	50.4 (4.63)	23.5 (1.21)	
ASP-197	118.6 (8.37)	176.0	54.0 (5.16)	41.7 (2.65 , 2.34)	
ILE-198	119.7 (7.92)	174.7	61.0 (4.32)	42.0 (1.49)	Cδ1 14.9 (0.60) Cγ1 27.1 (1.12) Cγ2 19.2 (0.93)
LYS-199	127.1 (9.18)	172.6	53.4 (4.53)	34.8 (1.54 , 1.36)	Cε 41.8 (2.88) Cδ 27.7 (1.62) Cγ 24.5 (1.22)
PRO-200					
ASP-201	123.2 (8.39)	179.3	51.3 (4.55)	40.3 (2.5 , 3.12)	
GLY-202			46.5 (3.43 , 3.71)		
LYS-203	120.3 (7.74)	174.9	55.1 (4.12)	31.2 (0.58 , 1.16)	Cδ 28.5 (1.42 , 1.32) Cγ 24.9 (1.08 , 1.02)
ARG-204	111.8 (8.06)	175.2	56.9 (3.44)	26.6 (2.15 , 2.10)	Cδ 41.7 (3.17) Cγ 26.7 (1.57)
HIS-205	120.3 (8.53)	174.9	53.7 (4.77)	27.8 (3.14 , 2.82)	Hδ2 6.50 Hε1 7.60
ALA-206	123.2 (8.49)	175.8	52.2 (4.62)	19.8 (1.21)	
VAL-207	123.2 (9.17)	173.4	60.8 (4.98)	35.5 (2.05)	Cγ1 21.2 (0.77) Cγ2 19.0 (0.71)
ILE-208	122.7 (8.89)	174.7	60.8 (4.31)	41.6 (1.35)	Cδ1 13.5 (0.67) Cγ1 27.1 (1.22 , 0.71) Cγ2 18.1 (0.65)
SER-209	122.1 (8.42)	173.0	55.7 (4.91)	64.4 (3.61 , 3.53)	
GLY-210	110.5 (7.29)	172.5	45.2 (4.43 , 3.35)		
SER-211	116.5 (8.65)	172.9	58.8 (5.03)	64.4 (3.84 , 3.64)	
VAL-212	117.1 (7.40)	174.5	58.8 (5.04)	30.5 (1.62)	Cγ1 24.4 (0.68) Cγ2 20.7 (0.61)
LEU-213	124.2 (8.96)	175.5	52.6 (5.31)	45.6 (1.59 , 1.03)	Cδ1 25.3 (0.73) Cδ2 22.9 (0.58) Cγ 27.3 (1.29)
TYR-214	120.2 (8.84)	176.0	56.9 (4.77)	41.7 (2.70 , 2.75)	Qδ 6.89 Qε 6.70
ASN-215	129.8 (9.29)	174.3	53.9 (4.00)	36.5 (2.21 , 2.75)	Nδ2 111.6 (7.01 , 6.48)
GLN-216	106.4 (8.61)	173.5	57.9 (3.45)	26.1 (2.29 , 2.19)	Cγ 34.0 (2.14) Nε2 112.5 (6.68 , 7.39)

ALA-217	123.3 (7.66)	176.4	50.8 (4.61)	20.5 (1.37)	
GLU-218	122.6 (8.71)	177.9	57.5 (4.53)	28.8 (1.98 , 2.09)	Cγ 36.2 (2.39 , 2.26)
LYS-219	126.9 (8.84)	173.8	53.1 (4.61)	34.2 (2.25 , 1.28)	Cδ 28.1 (1.58) Cε 41.9 (2.79) Cγ 24.5 (1.65 , 1.46)
GLY-220	107.0 (7.93)	173.9	44.5 (5.47 , 3.72)		
SER-221	117.3 (8.68)	171.0	56.8 (5.46)	66.7 (3.84 , 3.79)	
TYR-222	117.6 (8.96)	172.8	55.8 (5.39)	41.7 (2.63 , 2.43)	Qδ 6.30 Qε 6.20 HH 7.61
SER-223	115.6 (8.84)	173.1	56.6 (5.17)	64.5 (3.65 , 3.60)	
LEU-224	123.5 (9.30)	175.6	53.1 (4.75)	46.3 (1.18 , 0.93)	Cδ1 23.7 (-0.38) Cδ2 23.0 (-0.19) Cγ 25.4 (1.17)
GLY-225	109.0 (9.04)	171.5	43.8 (4.62 , 3.41)		
ILE-226	120.2 (6.85)	174.8	60.4 (4.62)	38.2 (1.37)	Cδ1 14.5 (0.71) Cγ 2 16.0 (1.00) Cγ1 27.8 (1.21)
PHE-227	128.2 (9.39)	175.1	58.1 (4.77)	42.5 (2.22 , 2.81)	Qδ 6.57 Qε 6.72
GLY-228	104.6 (8.68)		42.4 (3.17 , 4.31)		
GLY-229			46.9		
LYS-230	118.7 (8.37)	174.7	54.1 (4.30)	30.8 (1.82 , 1.04)	Cδ 28.6 (1.50)
ALA-231	118.1 (7.63)	176.7	51.9 (3.81)	16.1 (1.16)	
GLN-232	118.0 (9.39)	176.0	61.0 (3.88)	28.7 (1.84)	Cγ 31.7 (2.24)
GLU-233	116.6 (8.82)	174.9	54.3 (5.41)	33.8 (1.72)	Cγ 34.1 (2.17)
VAL-234	109.3 (8.34)	174.8	57.9 (5.54)	35.4 (1.47)	Cγ1 20.0 (-0.04) Cγ2 17.4 (0.04)
ALA-235	120.7 (8.47)	176.4	51.3 (4.94)	20.3 (1.05)	
GLY-236	111.1 (9.36)	170.1	46.2 (5.08 , 4.02)		
SER-237	115.3 (8.89)	171.4	56.5 (5.28)	66.4 (3.84 , 3.71)	
ALA-238	119.9 (9.08)	174.5	49.9 (5.15)	21.7 (1.02)	
GLU-239	122.7 (9.02)	174.1	54.8 (4.63)	31.4 (1.78)	Cγ 36.1 (2.04 , 1.87)
VAL-240	124.2 (8.81)	174.8	61.4 (4.39)	33.9 (1.61)	Cγ2 21.4 (0.65)
LYS-241	127.6 (8.84)	174.5	56.0 (3.98)	32.1 (1.45 , 1.64)	Cε 41.5 (2.81) Cγ 25.1 (1.20) Cδ 28.8 (1.55)
THR-242	114.5 (7.21)	176.5	61.1 (4.36)	72.6 (4.28)	Cγ2 21.3 (0.79)
VAL-243	120.7 (9.58)	176.2	64.7 (3.85)	31.0 (2.10)	Cγ1 20.1 (0.87)
ASN-244	115.6 (7.57)	173.8	52.0 (4.88)	39.2 (2.25 , 2.89)	Nδ2 113.6 (6.86 , 7.58)
GLY-245	107.7 (7.36)	174.3	43.3 (4.54 , 3.73)		
ILE-246	122.7 (8.67)	176.9	61.1 (4.35)	36.9 (1.63)	Cδ1 12.2 (0.72) Cγ 1 27.7 (1.48 , 1.03) Cγ2 17.3 (0.50)
ARG-247	128.5 (9.23)	173.9	53.5 (4.37)	31.9 (1.47)	Cδ 41.8 (3.02) Cγ 27.2 (1.79)
HIS-248	121.1 (8.52)	174.6	55.8 (5.32)	32.9 (2.94)	Hδ2 7.15 Hε1 7.70
ILE-249	119.4 (8.72)	176.2	58.5 (4.52)	42.0 (1.39)	Cδ1 13.9 (0.57) Cγ1 25.4 (1.22 , 0.73) Cγ2 17.8 (0.54)
GLY-250	113.7 (9.35)	171.0	44.2 (3.71 , 2.12)		
LEU-251	120.8 (7.83)	174.5	52.5 (4.72)	46.8 (0.78 , 1.03)	Cδ1 23.8 (0.59) Cδ2 25.7 (0.38) Cγ 26.3 (0.48)
ALA-252	122.9 (7.91)	173.4	51.5 (4.59)	21.5 (0.92)	
ALA-253	123.0 (9.04)	174.9	51.7 (4.73)	23.0 (0.93)	
LYS-254	115.7 (8.17)	175.1	53.9 (5.73)	36.3 (1.78 , 2.06)	Cε 40.4 (2.99) Cγ 22.6 (1.62)
GLN-255	122.7 (8.86)	176.6	57.1 (4.28)	29.5 (1.93 , 1.77)	Cγ 33.0 (2.04)
HIS-256	124.2 (8.62)	173.7	54.9 (4.58)		

Table S3. Statistical analysis of the energy minimized family of conformers of fHbp.

	fHbp[a] (30 Conformers)
Total number of meaningful NOE upper distance constraints	2987
Intra-protein NOEs[b]	
Intra-residue	481
Inter-residue	
Sequential (|i-j| = 1)	919
Medium-range (|i-j| < 4)	399
Long-range (|i-j > 5)	1188
Total meaningful dihedral angle restraints[b]	316
Phi	158
Psi	158
RMS violations per meaningful distance constraint (Å):	
Intraresidue	0.0205±0.0014
Sequential	0.0077±0.0009
Medium range	0.0101±0.00014
Long range	0.0085±0.0009
RMS violations per meaningful dihedral angle constraints (°):	
Phi	2.3646±1.2693
Psi	2.2273±1.3964
Average number of violations per conformer:	
Intraresidue	20.069 ±3.005
Sequential	14.586±2.871
Medium range	11.000±2.613
Long range	23.900±4.294
Phi	2.6000±1.1358
Psi	3.8500±1.3219
NOE violations larger than 0.3 Å	0.000
Average RMSD to the mean (Å)	
Residue range 14-255 (backbone atoms)	1.25±0.23
Residue range 14-255 (all heavy atoms)	1.75±0.21
Secondary structure elements (backbone atoms)	1.01±0.21
Secondary structure elements (all heavy atoms)	1.50 ±0.21
residual CYANA Target Function ($Å^2$)	2.13±0.44
Structural analysisc	
% of residues in most favorable regions	72.5
% of residues in allowed regions	23.1
% of residues in generously allowed regions	3.4
% of residues in disallowed regions	1.0
WHAT IF structure Z-scores[d]	
1st generation packing quality	-2.92
2st generation packing quality	-2.17
Ramachandran plot appearance	-3.62
χ_1/χ_2 rotamer normality	-3.72
Backbone conformation	0.71
WHAT IF RMS Z-scores[e]	

Bond lengths	0.63
Bond angles	1.17
Omega angle restraints	1.4
Side chain planarity	1.82
Improper dihedral distribution	1.01
Inside/Outside distribution	1.03
QUEEN	
I_{uni}/I_{total} (%) < 0.001	2507 (76%)
Average/SD	0.0016 ± 0.0054
Max	0.091

[a] Structure calculations were performed with the program CYANA 2.1 [Güntert, P. *et. al* J.Mol.Biol. 273, 1997]. A total of 900 random conformers were subjected to 13000 steps of a simulated annealing process. Each member of the family was submitted to restrained energy minimization (REM in explicit solvent) with the Amber-10 package [Case D.A. *et al* University of California: San Francisco, CA, 2008]. Values of 50 kcal mol-1 $Ã^{-2}$ and 32 kcal $mol^{-1}rad^{-2}$ were used as force constants for the NOE and torsion angle restraints, respectively. The data are calculated over the 30 conformers representing the NMR structure and on the energy minimized mean structure. The mean value and the standard deviation are given

[b] Number of meaningful constraints for each class. Backbone dihedral angle constraints were derived from ^{15}N,$^{13}C'$,$^{13}C\alpha$,$^{13}C\beta$, and Ha chemical shifts, using TALOS and added as restrains in the structure calculations as well.

[c] As it results from the Ramachandran plot analysis performed with PROCHECK.

[d] Values calculated on secondary structure elements. A Z-score is defined as the deviation from the average value for this indicator observed in a database of high-resolution crystal structures, expressed in units of the standard deviation of this database-derived average. Typically, Z-scores below a value of -3 are considered poor, those below -4 are considered bad.

[e]Values calculated on all residues.

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