Supporting Information

Murine Interleukin-3: Structure, Dynamics and Conformational Heterogeneity in Solution

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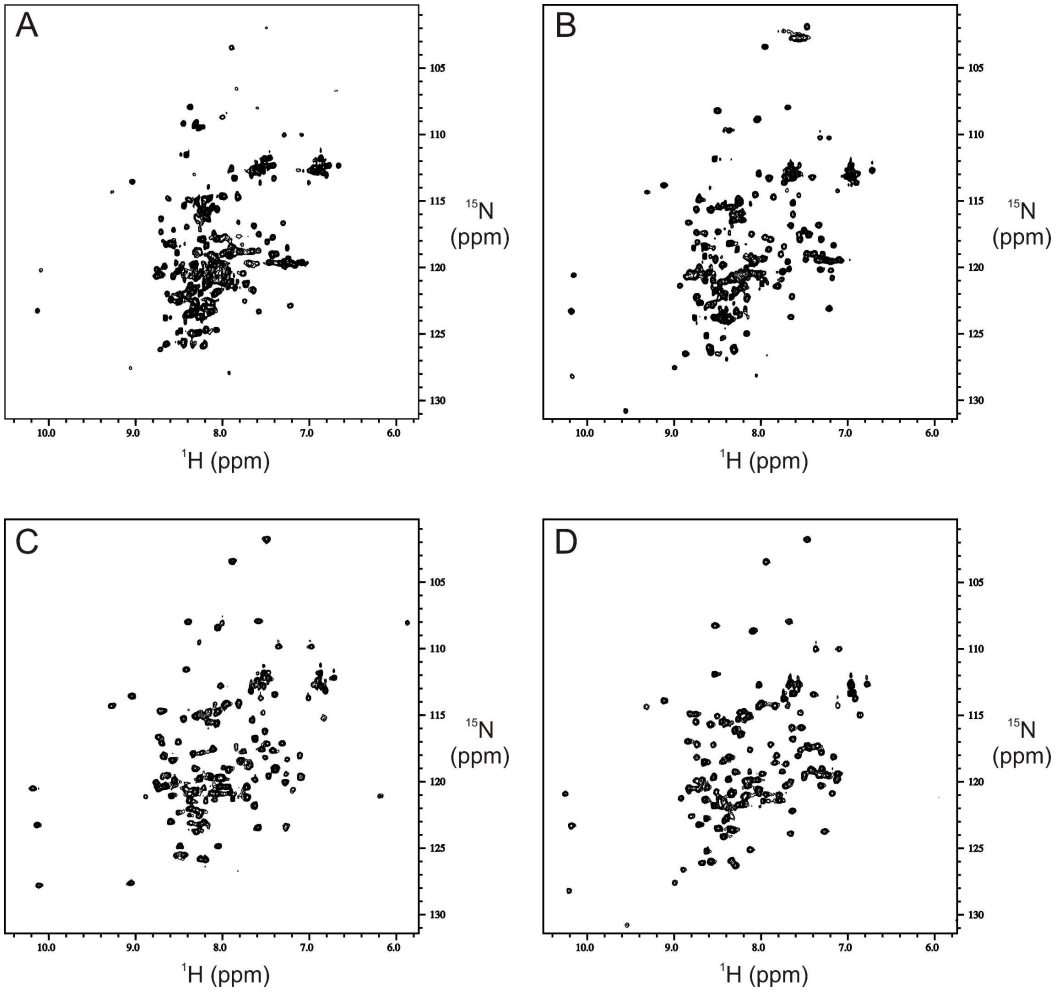


Figure S1. $^{1}H^{-15}N$ HSQC spectra of mIL-3_{33-156} in 0.2 mM acetate buffer, pH 4.3 at 298 K (A), 283 K (B), and in 20 mM potassium phosphate buffer, pH 6.7 at 298 K (C), 283 K (D), respectively. All spectra were recorded at 500 MHz using a Bruker Avance500 spectrometer equipped with a cryoprobe (NS=24).

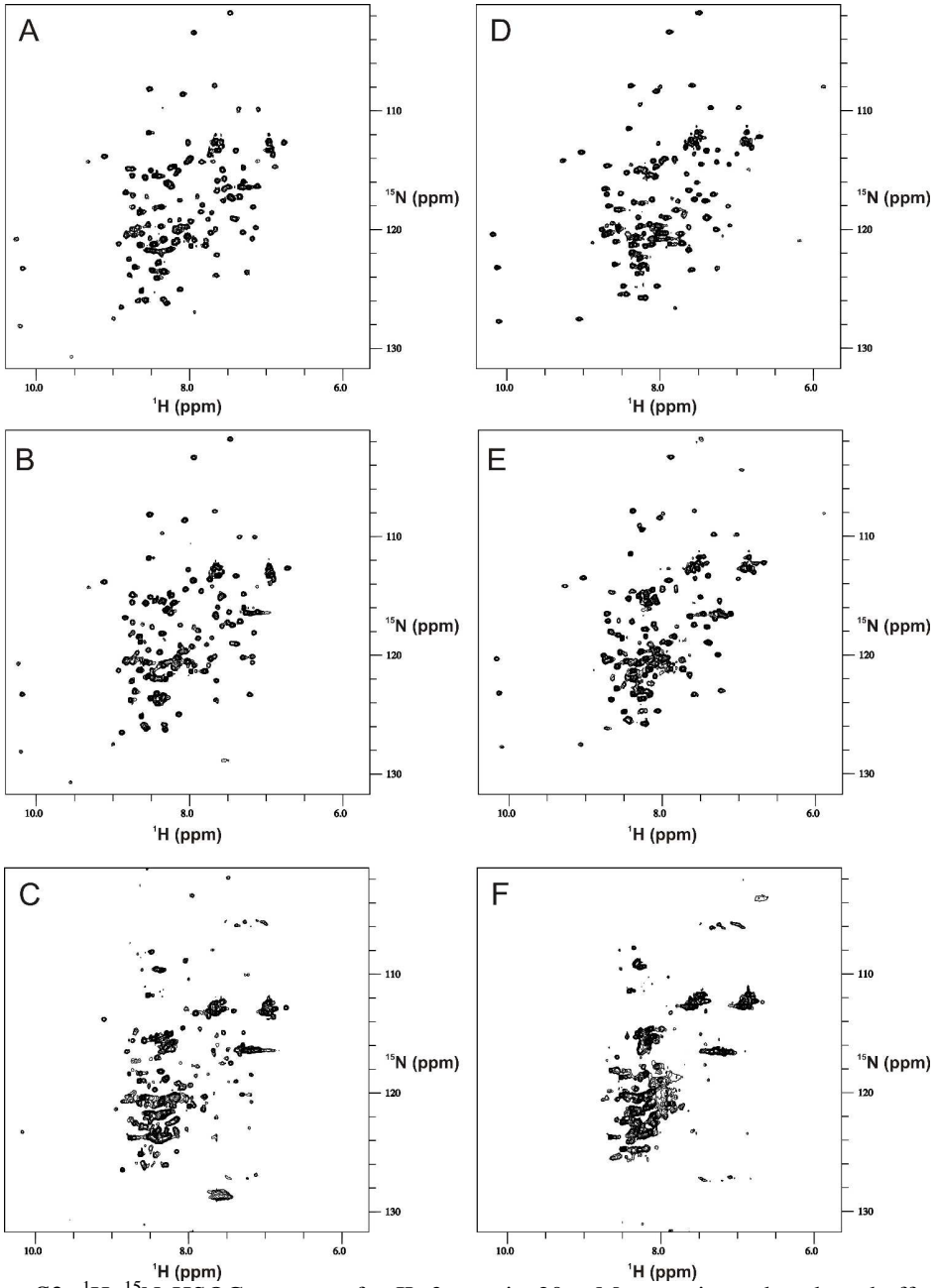


Figure S2. ^{1}H $^{-15}$N HSQC spectra of mIL-$3_{33\text{-}156}$ in 20 mM potassium phosphate buffer, pH 6.7(A) 283K, 0.22 mM, (B) 283 K, 0.30 mM, (C) 283 K, 0.44 mM, (D) 298 K, 0.22 mM, (E) 298K, 0.30 mM, and (F) 298 K 0.44 mM. All spectra were recorded at 500 MHz using a Bruker Avance500 spectrometer equipped with a cryoprobe (NS=24).

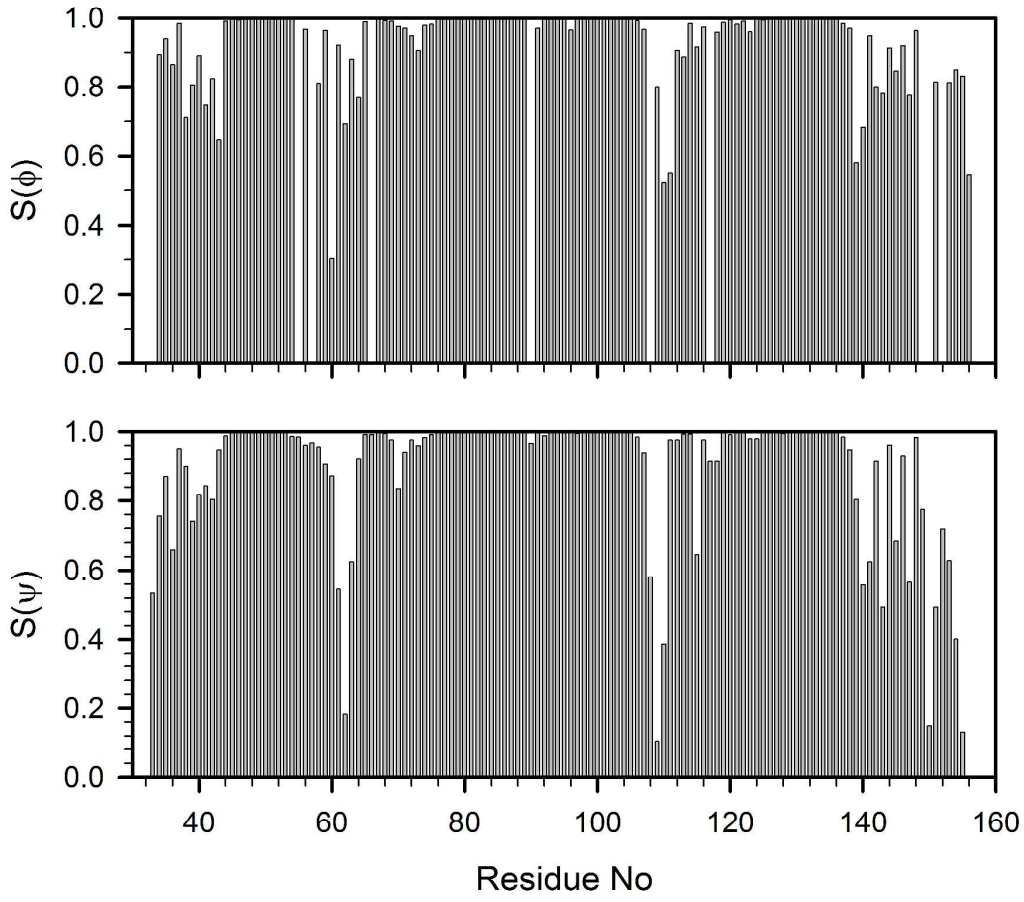


Figure S3. Summary of backbone angular order parameters of mIL-$3_{33\text{-}156}$ ensemble in 20 mM potassium phosphate, pH 6.7 and 283 K.

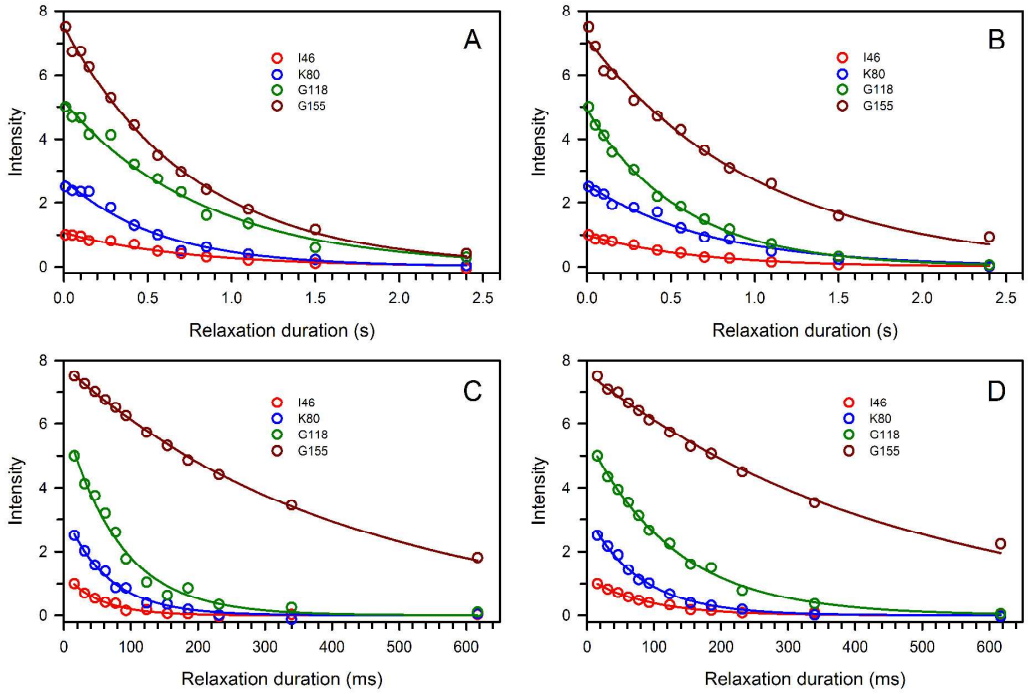
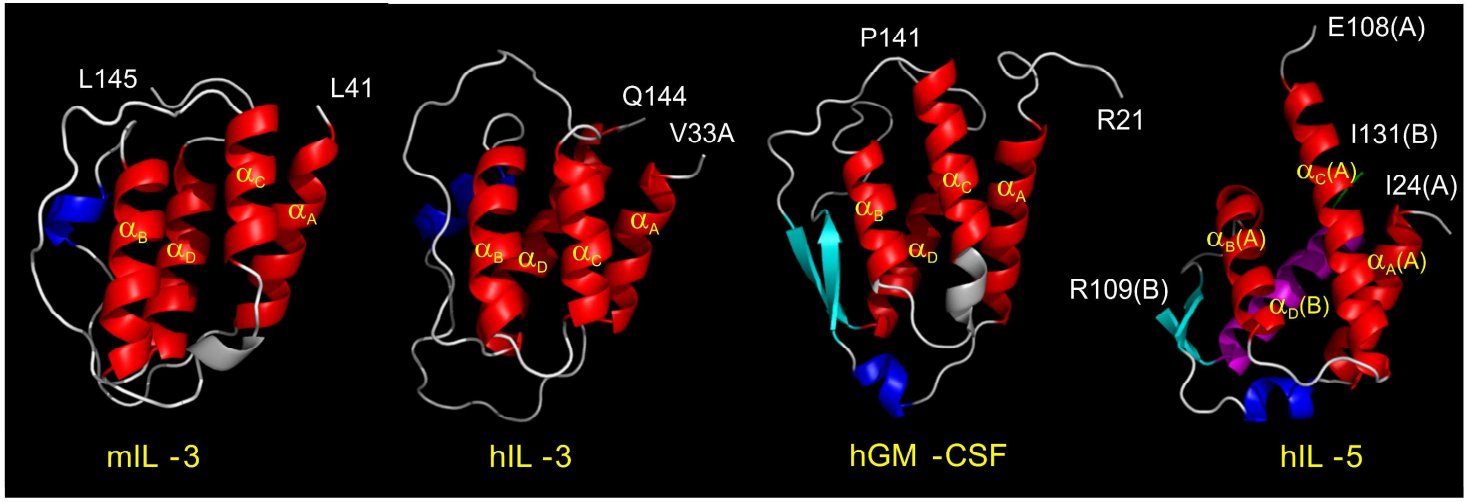


Figure S4. Backbone ^{15}N relaxation decay curves for representative residues of mIL-3$_{33\text{-}156}$. (A) R_1 at 283K, (B) R_1 at 298 K, (C) R_2 at 283 K, and (D) R_2 at 298 K. Lines represent the results of nonlinear regression of a two-parameter single exponential decay.

A



B

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mIL-3(33-70)          DTHRLTRTLNCSSIVKEIIGKLPEP--------ELKTDDEGPSLRN
hIL-3(33-70)                VNCSNMIDEIITHLKQPPLPLLDFNNLNGEDQDILMEN
hGM-CSF(18-67)   APARSPSPSTQPWEHVNAIQEARRLLNLSRDTAAEMNETVEVISEMFDLQ
hIL-5(24-59)                IPTSALVKETLALLSTHRTLLIA-NETL-RIPVPVHKN

mIL-3(71-114)         -KSFRRVNLSKFVESQGEVD-PEDRYVIKSNLQKLNCCLPTSANDS
hIL-3(71-111)         --NLRRPNLEAFNRAVKSLQ---NASAIESILKNLLPCLPLATAAP
hGM-CSF(68-108)       EPTCLQTRLELYKQGL-----RGSLTKLKGPLTMMASHYKQHCPPT
hIL-5(60-105)         HQLCTEEIFQGIGTLESQTVQGGTVERLFKNLSLIKKYIDGQKKKC

mIL-3(115-156)        ALPGVFIR--DLDDFRKKLRFYMVHLNDLETVLTSRPPQPASGS
hIL-3(112-144)        TRHPIHIKDGDWNEFRRKLTFYLKTLENAQAQQ
hGM-CSF(109-144)      PETSCATQIITFESFKENLKDFLLVIPFDCWEPVQE
hIL-5(106-131)        G-----EERRRVNQFLDYLQEFLGVMNTEWI
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Figure S5. Structures and sequence alignments of mIL-3, hIL-3, GM-CSF, and hIL-5. (A) Ribbon diagram of murine IL-3, human IL-3 analogue (pdb code: 1JLI), human GM-CSF (pdb code: 2GMF), and human IL-5 (pdb code: 1HUL). For human IL-5, only residues of 5-89 of chain A and 90-112 of Chain-B are shown. These figures were generated using the program PyMOL (DeLano 2004; http://pymol.sourceforge.net). (B) Sequence alignments of mIL-3 (SwissProt No: P01586, showing residues 33-156), hIL-3 analogue (SwissProt No: P08700, showing residues; 33-144), GM-CSF (SwissProt No: P04141, showing residues 18-144), and hIL-5 (SwissProt No: P05113, showing residues 24-131) based on experimentally defined four helices. Conserved residues are highlighted in yellow. Residues mutated in structural studies of mIL-3 and hIL-3 are underlined. Four main α-helical regions are coded in red whereas the short helix located within the α_A-α_B loop is coded in blue. Regions of β-hairpin as observed in the crystal structures of hIL-5 and human GM-CSF are highlighted in cyan and the single-turn helices within the α_C-α_D loops of mIL-$3_{33\text{-}156}$ and GM-CSF in grey.

Table S1 ^{15}N NMR relaxation parameters measured at $\omega_N = 2\pi \times 60.81$ MHz for mIL-$3_{33\text{-}156}$ in phosphate buffer, pH 6.7

Residue	Sequence No	283 K						298 K					
		R_1 (s^{-1})	ΔR_1 (s^{-1})	R_2 (s^{-1})	ΔR_2 (s^{-1})	NOE	ΔNOE	R_1 (s^{-1})	ΔR_1 (s^{-1})	R_2 (s^{-1})	ΔR_2 (s^{-1})	NOE	ΔNOE
ASP	33	1.70	0.04	3.18	0.06	-0.21	0.01	2.00	0.07	2.67	0.13	-0.45	0.04
THR	34	1.74	0.05	5.34	0.19	-0.06	0.01	1.50	0.07	4.26	0.24	-0.24	0.05
HIS	35	1.98	0.11	5.65	0.32	0.21	0.02						
ARG	36	1.86	0.07	5.56	0.19	0.15	0.02	2.13	0.25	4.28	0.3	-0.16	0.07
LEU	37	1.77	0.07	5.50	0.31	0.19	0.02	1.98	0.09	4.37	0.23	0.05	0.04
THR	38	1.85	0.07	8.04	0.21	0.26	0.02	1.68	0.12	5.91	0.36	0.08	0.04
ARG	39	1.54	0.11	8.43	0.39	0.26	0.03	1.96	0.18	7.18	0.41	0.13	0.06
THR	40	1.58	0.06	10.17	0.44	0.40	0.02	1.93	0.13	8.28	0.52	0.31	0.03
LEU	41	1.54	0.09	10.50	0.73	0.55	0.11	1.62	0.20	10.17	3.11	0.32	0.08
ASN	42												
CYS	43	1.31	0.09	12.26	1.08	0.73	0.06	1.74	0.19	10.53	1.05	0.66	0.10
SER	44	1.08	0.07	20.29	0.99	0.67	0.06	1.43	0.2	13.74	1.15	0.85	0.10
SER	45	1.07	0.10	19.40	2.33	0.68	0.09	1.81	0.44	19.61	4.66	0.78	0.16
ILE	46	1.36	0.11	19.10	1.36	1.04	0.12	1.59	0.07	11.37	0.46	0.70	0.04
VAL	47	0.82	0.06	18.32	1.43	0.77	0.07	1.32	0.09	10.78	0.59	0.83	0.03
LYS	48	1.27	0.13	22.06	2.21	0.86	0.07	1.76	0.11	13.67	0.38	0.64	0.03
GLU	49	1.58	0.16	17.57	1.11	0.67	0.05	1.79	0.14	11.86	0.79	0.66	0.07
ILE	50	1.03	0.10	21.59	1.08	1.07	0.11	1.34	0.09	11.32	0.44	0.83	0.03
ILE	51	1.08	0.10	26.62	1.84	0.80	0.09	2.05	0.09	14.12	0.33	0.68	0.04
GLY	52	1.02	0.08	17.95	1.50	0.75	0.07	1.62	0.12	15.27	0.82	0.80	0.05
LYS	53	1.30	0.11	18.63	1.36	0.88	0.06	1.82	0.08	12.07	0.33	0.70	0.02
LEU	54	1.43	0.06	26.41	4.67	0.78	0.06	1.88	0.08	14.57	0.52	0.70	0.03
PRO	55												
GLU	56	1.53	0.12	13.65	0.62	0.70	0.05	1.61	0.06	8.83	0.23	0.62	0.03
PRO	57												
GLU	58	1.89	0.15	12.01	0.37	0.53	0.06	1.77	0.05	8.33	0.22	0.30	0.02
LEU	59	1.30	0.06	12.04	0.66	0.42	0.04	1.94	0.05	9.90	0.33	0.52	0.02
LYS	60	1.36	0.05	15.24	0.54	0.35	0.04	1.76	0.06	7.47	0.39	0.19	0.03
THR	61	1.53	0.09	14.23	0.43	0.39	0.04	1.77	0.06	8.53	0.37	0.30	0.03
ASP	62	1.75	0.06	11.47	0.29	0.48	0.02	1.78	0.14	8.55	0.63	0.47	0.06
ASP	63												
GLU	64												
GLY	65	1.41	0.11	12.72	0.48	0.61	0.06	1.71	0.13	8.02	0.59	0.42	0.06
PRO	66												
SER	67	1.26	0.07	19.69	1.22	0.63	0.06	2.42	0.31	15.12	1.86	0.21	0.10
LEU	68	1.12	0.19	22.36	3.90	0.71	0.09					0.73	0.26

ARG	69	1.36	0.18	25.17	2.90	0.61	0.12					0.38	0.39
ASN	70	1.47	0.20	16.18	1.78	0.64	0.10						
LYS	71	1.46	0.24	35.47	7.89	0.75	0.16						
SER	72	1.30	0.07	20.72	2.06	0.88	0.10					0.24	0.15
PHE	73	1.40	0.12	18.26	2.44	0.78	0.13					0.44	0.15
ARG	74	1.98	0.21	14.31	1.76	1.01	0.14					0.58	0.13
ARG	75	1.49	0.19	22.72	1.76	0.76	0.10					0.73	0.25
VAL	76	1.48	0.32	26.48	6.75	0.95	0.12			10.04	1.45	0.43	0.11
ASN	77	1.44	0.15	19.90	3.67	0.96	0.10	1.89	0.06	11.72	0.36	0.76	0.03
LEU	78	1.39	0.16	24.59	2.52	0.92	0.12	1.85	0.16	9.96	0.98	0.67	0.12
SER	79	1.62	0.18	18.52	1.29	1.05	0.08	1.64	0.30	13.76	2.93	0.42	0.14
LYS	80	1.76	0.14	15.26	0.84	0.78	0.07	1.34	0.09	12.45	0.46	0.57	0.04
PHE	81	1.69	0.09	15.98	0.68	0.75	0.04						
VAL	82	0.99	0.09	18.73	2.93	0.71	0.10						
GLU	83	1.53	0.15	16.57	1.36	0.77	0.07	1.87	0.06	12.19	0.42	0.72	0.03
SER	84	1.20	0.12	20.60	0.95	0.76	0.06	1.83	0.17	14.75	1.17	0.62	0.06
GLN	85	1.73	0.18	12.76	0.52	0.89	0.08						
GLY	86	1.49	0.13	17.86	1.17	0.51	0.07	1.53	0.19	16.97	1.58	0.78	0.08
GLU	87	1.28	0.06	19.26	0.54	0.81	0.05	1.68	0.10	12.11	0.40	0.65	0.03
VAL	88	0.92	0.10	19.10	1.67	0.62	0.08	1.13	0.16	16.11	0.71	0.55	0.08
ASP	89	1.29	0.06	17.85	0.73	0.80	0.04	1.60	0.07	10.95	0.39	0.63	0.02
PRO	90												
GLU	91	0.91	0.06	22.28	1.12	0.66	0.06	1.28	0.09	12.89	0.60	0.71	0.05
ASP	92	1.25	0.14	14.06	1.35	0.96	0.08	1.57	0.08	11.47	0.37	0.89	0.05
ARG	93	1.22	0.08	16.77	0.71	0.69	0.07	1.69	0.06	12.66	0.59	0.66	0.03
TYR	94	1.07	0.14	22.42	2.95	0.62	0.10	1.67	0.09	10.67	0.53	0.80	0.08
VAL	95	1.03	0.11	15.76	1.65	0.76	0.05	1.77	0.12	10.64	0.68	0.50	0.05
ILE	96	1.91	0.30	18.47	2.23	0.52	0.10	1.36	0.17	15.74	1.38	0.73	0.08
LYS	97	1.41	0.21	17.03	1.93	1.02	0.14	2.37	0.13	16.68	1.56	0.60	0.06
SER	98	1.43	0.13	19.84	1.04	0.81	0.06	1.73	0.08	11.96	0.52	0.66	0.04
ASN	99	0.84	0.06	17.37	1.17	0.80	0.05	1.80	0.03	11.08	0.26	0.81	0.03
LEU	100	1.30	0.13	17.89	2.72	0.45	0.09	2.84	0.81	21.01	4.11	0.66	0.13
GLN	101	1.99	0.25	23.31	1.77	0.98	0.14	2.09	0.37	18.28	3.67	0.89	0.19
LYS	102	1.19	0.06	17.44	1.01	0.60	0.05	1.56	0.07	12.03	0.62	0.72	0.04
LEU	103	1.13	0.12	24.09	3.82	0.88	0.13						
ASN	104	1.51	0.14	18.27	1.29	0.85	0.08	2.18	0.29	16.67	2.18	0.96	0.15
ALA	105	0.92	0.12	17.66	0.72	0.62	0.04	1.88	0.13	13.38	0.47	0.65	0.03
CYS	106	1.52	0.15	19.32	1.22	0.67	0.06	1.82	0.14	21.72	1.35	0.52	0.09
LEU	107	1.30	0.12	17.39	2.41	0.73	0.11						
PRO	108												

THR	109	1.20	0.05	16.3	0.5	0.61	0.04	1.65	0.06	10.51	0.25	0.55	0.03
SER	110	1.31	0.12	14.84	1.24	0.67	0.05	1.82	0.10	8.84	0.31	0.42	0.04
ALA	111	1.44	0.1	13.81	0.63	0.45	0.06						
ASN	112	1.75	0.11	13.07	0.35	0.47	0.04						
ASP	113	1.27	0.157	13.54	0.99	0.45	0.04	2.15	0.53	26.18	5.07	0.62	0.13
SER	114	1.65	0.13	19.2	0.94	0.48	0.05	2.00	0.27	18.40	1.79	0.40	0.09
ALA	115	1.51	0.09	15.93	0.87	0.49	0.05	1.93	0.08	10.25	0.78	0.57	0.04
LEU	116	1.19	0.08	13.94	0.76	0.59	0.06	1.34	0.07	8.87	0.36	0.51	0.03
PRO	117												
GLY	118	1.20	0.07	12.33	0.82	0.56	0.04	1.77	0.05	7.76	0.21	0.53	0.03
VAL	119	1.18	0.10	17.46	1.08	0.55	0.07	1.66	0.18	12.98	1.24	0.63	0.20
PHE	120	1.13	0.09	17.01	1.33	0.61	0.07	1.45	0.17	12.29	1.11	0.65	0.08
ILE	121	1.19	0.10	18.25	1.72	0.61	0.05	1.60	0.07	12.25	0.38	0.71	0.04
ARG	122	1.18	0.15	20.62	1.72	0.71	0.13	2.03	0.20	11.55	1.04	0.65	0.09
ASP	123	1.24	0.14	15.63	0.70	0.64	0.06	1.92	0.08	11.16	0.26	0.67	0.03
LEU	124	1.54	0.17	15.80	1.82	0.67	0.06	1.80	0.11	11.05	0.36	0.73	0.04
ASP	125	0.93	0.05	17.42	1.08	0.73	0.05	1.48	0.05	11.22	0.42	0.81	0.02
ASP	126	1.80	0.16	16.23	1.42	0.99	0.06	1.89	0.06	11.72	0.36	0.76	0.03
PHE	127	1.09	0.10	19.57	2.25	0.58	0.10	1.53	0.10	12.46	0.67	0.64	0.06
ARG	128	1.31	0.11	22.48	1.85	0.71	0.08	1.53	0.11	12.35	0.33	0.72	0.04
LYS	129	1.68	0.14	20.41	1.18	0.85	0.07	1.68	0.11	12.09	0.46	0.62	0.03
LYS	130	1.22	0.08	18.55	1.15	0.91	0.08	1.61	0.08	12.01	0.61	0.81	0.05
LEU	131	1.01	0.01	19.63	1.29	0.80	0.07	1.67	0.10	11.35	0.41	0.79	0.02
ARG	132	1.64	0.10	16.20	0.95	0.84	0.08	1.75	0.11	12.66	0.45	0.85	0.05
PHE	133	1.76	0.18	18.19	1.42	0.69	0.08	1.40	0.13	13.43	0.71	0.73	0.07
TYR	134	1.13	0.23	13.48	6.97	0.83	0.15						
MET	135	1.04	0.15	27.81	3.86	0.66	0.10						
VAL	136	0.87	0.07	24.22	2.31	0.90	0.10	1.40	0.10	15.46	0.62	0.69	0.05
HIS	137	1.44	0.12	20.32	2.07	0.77	0.11			10.49	1.92	0.35	0.16
LEU	138	1.97	0.19	17.94	1.32	0.82	0.10	2.75	0.81	15.66	1.83	0.58	0.12
ASN	139	1.37	0.09	19.74	0.97	0.50	0.05	1.79	0.24	10.26	1.01	0.66	0.16
ASP	140	1.74	0.17	17.49	1.38	0.49	0.07	1.93	0.18	11.95	1.38	0.46	0.08
LEU	141	1.25	0.08	14.08	1.51	0.68	0.09	1.91	0.07	11.85	0.57	0.70	0.03
GLU	142	1.81	0.09	8.53	0.39	0.24	0.02	1.60	0.34	13.8	1.41	0.39	0.08
THR	143	1.46	0.06	13.75	0.83	0.38	0.04	1.80	0.11	10.18	0.42	0.54	0.04
VAL	144	1.86	0.11	12.00	0.72	0.46	0.02	1.92	0.11	8.44	0.32	0.31	0.03
LEU	145	1.53	0.10	12.24	0.62	0.39	0.04	1.82	0.17	9.80	0.60	0.40	0.07
THR	146	1.45	0.06	11.27	0.47	0.30	0.04						
SER	147	1.63	0.06	9.23	0.31	0.28	0.03	2.03	0.14	6.75	0.45	0.24	0.05
ARG	148	1.67	0.06	6.23	0.42	0.23	0.02	1.81	0.08	4.75	0.41	0.07	0.02

PRO	149												
PRO	150												
GLN	151	1.52	0.03	4.31	0.06	0.06	0.02	1.60	0.05	3.08	0.05	-0.14	0.01
PRO	152												
ALA	153	1.43	0.02	2.90	0.25	-0.26	-0.01	1.51	0.04	2.59	0.07	-0.74	0.02
SER	154	1.49	0.03	3.19	0.11	-0.62	-0.01	2.00	0.29	4.56	0.52	-0.82	0.10
GLY	155	1.30	0.03	2.44	0.03	-0.99	-0.01	0.97	0.04	2.20	0.07	-1.78	0.04
SER	156	0.83	0.02	1.21	0.02	-1.17	-0.01	0.7	0.02	0.095	0.02	-2.37	0.03

Table S2 Dynamics parameters for mIL-$3_{33\text{-}156}$ resulting from *Modelfree* analysis (anisotropic model - I) [a]

	283 K									298K								
No	**Model[b]**	χ^2	S_f^2	ΔS_f^2	τ_i	$\Delta\tau_i$	R_{ex}	ΔR_{ex}	S_s^2	ΔS_s^2	**Model[b]**	χ^2	S_f^2	ΔS_f^2	τ_i	$\Delta\tau_i$	R_{ex}	ΔR_{ex}	S_s^2	ΔS_s^2
					(ns)		(s^{-1})								(ns)		(s^{-1})			
33	5	0.000	0.09	0.01	0.94	0.01			0.91	0.02	5	0.000	0.04	0.02	0.86	0.02			1.11	0.04
34	2	1.855	0.22	0.01	0.97	0.01					5	0.000	0.30	0.03	0.76	0.05			0.88	0.04
35	2	0.124	0.20	0.02	1.28	0.03														
36	2	2.511	0.20	0.01	1.20	0.02					2	1.528	0.18	0.03	0.97	0.06				
37	5	0.000	0.25	0.02	1.22	0.03			0.91	0.03	2	0.055	0.23	0.03	1.07	0.06				
38	2	0.245	0.37	0.01	1.23	0.03					2	1.003	0.44	0.04	0.86	0.08				
39	5	0.000	0.46	0.04	1.14	0.06			0.91	0.04	2	1.642	0.45	0.04	0.98	0.10				
40	2	2.268	0.57	0.03	1.21	0.05					2	2.045	0.61	0.06	0.92	0.15				
41	2	2.013	0.61	0.04	1.28	0.25					2	0.078	0.76	0.11	0.53	0.39				
42																				
43	5	0.000	0.80	0.08	2.39	2.99			0.86	0.05	1	2.562	0.95	0.06						
44	4	0.000	0.94	0.04	0.13	0.38	3.14	1.23			1	0.091	1.00	0.04						
45	1	2.869	1.00	0.04							1	2.472	1.00	0.13						
46	6(4)	3.389	0.90	0.09	11.04	4.75	3.52	1.60			2	2.551	0.94	0.03	0.14	0.38				
47	3	0.586	0.66	0.05			7.28	1.65			1	1.076	0.85	0.03						
48	1	5.044	1.00	0.05							4	0.000	0.75	0.08	1.66	0.44	3.26	0.81		
49	4	0.000	0.75	0.10	1.88	0.64	4.42	1.70			1	5.389	1.00	0.03						
50	6(3)	5.025	0.82	0.08			8.12	1.75			3	0.375	0.78	0.05			2.36	0.78		
51	3	0.074	0.91	0.08			11.02	2.36			4	0.000	0.59	0.08	2.68	0.75	4.98	0.75		
52	1	2.270	0.94	0.04							3	0.500	1.00	0.05			2.34	1.16		
53	1	4.783	1.00	0.04							4	0.000	0.89	0.05	1.12	0.63	1.92	0.45		
54	4	0.000	0.89	0.06	2.76	3.86	11.29	4.47			4	0.000	0.79	0.06	2.00	0.49	4.54	0.68		
55																				
56	2	0.646	0.91	0.05	1.19	1.82					2	2.546	0.84	0.02	0.09	0.13				
57																				
58	2	2.785	0.64	0.03	1.62	0.31					2	0.774	0.67	0.02	0.72	0.07				
59	5	0.000	0.64	0.03	1.24	0.10			0.90	0.03	4	0.000	0.54	0.04	1.65	0.09	1.57	0.53		
60	4	0.000	0.68	0.04	0.98	0.08	1.82	0.81			2	0.278	0.50	0.04	0.96	0.07				
61	4	0.000	0.73	0.07	0.80	0.25	3.57	0.82			2	2.929	0.77	0.03	0.33	0.14				
62	2	1.167	0.54	0.02	1.54	0.06					2	0.015	0.68	0.07	1.07	0.31				
63																				

64																			
65	2	3.742	0.64	0.03	1.63	0.27				2	1.183	0.50	0.05	1.35	0.16				
66																			
67	4	0.000	0.93	0.04	0.22	0.37	4.59	1.35		6(4)	0.117	0.00	0.18	1.50	0.29	12.02	2.18		
68	1	4.110	1.00	0.08															
69	4	0.000	0.78	0.11	1.49	2.67	9.86	3.36											
70	1	4.232	1.00	0.06															
71	1	7.128	1.00	0.11															
72	6(4)	0.359	0.87	0.06	11.04	4.55	4.81	2.12											
73	2	0.179	0.76	0.08	4.24	3.58													
74	2	4.625	0.61	0.18	6.35	3.65													
75	3	4.133	1.00	0.10	0.00	0.00	3.73	2.92											
76	1	3.783	1.00	0.13															
77	1	4.099	1.00	0.06						4	0.000	0.89	0.05	2.34	1.72	1.40	0.49		
78	3	1.357	1.00	0.09			7.19	2.96		1	4.733	0.96	0.05						
79	6(4)	8.971	0.63	0.19	11.04	3.97	4.90	1.94		2	1.748	0.84	0.14	0.31	0.70				
80	2	3.132	0.77	0.09	4.26	3.52				4	0.000	0.72	0.05	0.05	0.02	4.11	0.72		
81	4	0.000	0.75	0.08	3.06	2.45	3.03	0.87											
82	1	4.666	0.83	0.07															
83	1	3.893	1.00	0.04						4	0.000	0.84	0.05	1.92	0.81	1.98	0.59		
84	3	1.118	0.96	0.07			4.73	1.91		4	0.000	0.80	0.11	1.20	0.86	5.12	1.39		
85	2	1.121	0.52	0.08	11.04	3.27	0.00	0.00											
86	4	0.000	0.73	0.09	1.14	0.33	5.20	1.57		3	0.151	0.88	0.09	0.00	0.00	6.87	2.05		
87	4	0.000	0.94	0.05	3.89	4.33	2.70	0.66		4	0.000	0.93	0.05	0.26	0.51	1.29	0.55		
88	4	0.000	0.69	0.07	0.02	0.01	7.79	2.08		4	0.000	0.64	0.09	0.03	0.02	8.45	1.28		
89	1	3.754	1.00	0.02						2	0.031	0.91	0.02	0.20	0.26				
90																			
91	4	0.000	0.88	0.05	0.05	0.79	4.57	1.57		1	4.971	0.92	0.04						
92	1	3.395	0.92	0.06						1	2.385	0.95	0.02						
93	1	4.290	0.99	0.03						4	0.000	0.86	0.05	1.10	0.41	1.95	0.71		
94	1	5.352	1.00	0.06						6(5)	0.018	0.67	0.05	7.34	2.21			0.93	0.04
95	1	4.669	0.87	0.06						2	1.602	0.86	0.04	0.41	0.31				
96	4	0.000	0.43	0.19	1.81	0.61	8.35	3.64		1	2.941	1.00	0.05						
97	1	2.561	1.00	0.06						4	0.000	0.33	0.12	2.47	0.50	10.16	1.94		
98	4	0.000	0.86	0.12	6.51	4.10	4.63	1.42		2	4.463	0.94	0.03	0.33	0.55				

99	3	0.215	0.67	0.05			6.31	1.46			2	0.108	0.89	0.03	7.34	2.11				
100	2	1.660	0.88	0.06	0.36	0.35					6(4)	0.012	0.00	0.31	3.94	2.19	16.02	4.25		
101	6(4)	1.640	0.21	0.22	10.94	3.90	12.93	2.42			1	4.445	1.00	0.11						
102	4	0.000	0.88	0.04	0.10	0.15	3.12	1.19			4	0.000	0.86	0.04	0.04	0.03	2.27	0.72		
103	1	5.129	0.98	0.06																
104	1	5.347	1.00	0.03							6(4)	1.477	0.54	0.24	7.34	2.40	7.45	2.83		
105	4	0.000	0.69	0.10	0.02	0.02	6.25	1.81			4	0.000	0.79	0.10	1.46	0.64	3.84	0.85		
106	4	0.000	0.78	0.09	1.77	1.04	5.51	1.72			4	0.000	0.68	0.13	1.26	0.87	12.75	1.74		
107	1	0.978	1.00	0.05																
109	2	0.006	0.87	0.02	0.99	0.22					2	0.257	0.89	0.02	0.34	0.18				
110	2	0.312	0.83	0.06	1.53	0.49					2	0.174	0.56	0.03	1.33	0.12				
111	4	0.000	0.80	0.07	0.70	0.31	1.87	0.97												
112	2	2.823	0.59	0.02	1.52	0.13														
113	2	2.504	0.86	0.04	0.26	0.25					3	2.222	1.00	0.17	0.00	0.00	15.23	6.17		
114	4	0.000	0.55	0.08	1.54	0.18	7.02	1.51			4	0.000	0.40	0.21	1.50	0.39	11.41	2.48		
115	4	0.000	0.75	0.07	0.99	0.27	4.27	1.23			2	3.637	0.89	0.04	0.43	0.34				
116	4	0.000	0.81	0.06	0.06	0.08	2.20	1.11			4	0.000	0.64	0.04	0.05	0.01	2.45	0.48		
118	5	0.000	0.77	0.04	1.23	0.19			0.87	0.04	5	0.000	0.61	0.03	1.50	0.13			0.92	0.02
119	4	0.000	0.85	0.06	0.10	0.26	4.03	1.50			1	1.621	1.00	0.04						
120	2	0.043	0.89	0.04	0.88	0.44					2	0.081	0.86	0.07	1.14	1.34				
121	2	0.447	0.87	0.05	1.04	0.42					2	0.240	0.88	0.03	1.55	0.86				
122	1	3.468	1.00	0.05							1	5.582	1.00	0.04						
123	2	0.158	0.84	0.04	1.30	0.46					4	0.000	0.74	0.07	1.90	0.39	1.72	0.54		
124	2	0.922	0.82	0.07	1.69	1.08					1	4.619	0.98	0.02						
125	3	3.492	0.75	0.04			5.01	1.26			3	0.002	0.85	0.03			1.53	0.54		
126	6(4)	9.390	0.45	0.19	11.04	3.53	4.36	1.73			4	0.000	0.85	0.05	2.81	1.83	1.35	0.50		
127	4	0.000	0.80	0.07	0.06	0.09	6.73	2.49			4	0.000	0.82	0.06	0.06	0.07	3.26	0.90		
128	3	2.324	1.00	0.05	0.00	0.00	5.36	2.20			4	0.000	0.86	0.06	0.04	0.21	2.32	0.77		
129	6(4)	0.355	0.52	0.16	11.04	3.74	7.65	1.48			2	3.410	0.92	0.03	0.35	0.31				
130	3	1.194	0.93	0.05			3.86	1.43			1	2.327	0.98	0.02						
131	3	0.108	0.80	0.01			6.49	1.30			1	1.065	0.98	0.02						
132	2	4.528	0.82	0.07	4.88	3.63	0.00	0.00			1	4.538	1.00	0.02						
133	4	0.000	0.65	0.15	2.46	2.47	5.82	2.05			1	5.981	1.00	0.03						
134	1	0.012	0.87	0.14																

135	3	2.659	0.82	0.12			14.24	4.63												
136	3	0.582	0.71	0.05			12.38	2.45			4	0.000	0.82	0.06	0.04	0.16	5.67	0.94		
137	4	0.000	0.89	0.09	2.35	4.43	5.56	2.15												
138	6(5)	0.009	0.60	0.10	11.04	3.86					4	0.000	0.00	0.28	2.78	1.51	11.44	2.56		
139	4	0.000	0.75	0.06	1.11	0.20	5.70	1.37			1	2.387	0.92	0.07						
140	4	0.000	0.61	0.12	1.33	0.32	7.74	1.86			4	0.000	0.72	0.15	0.85	0.49	4.44	1.75		
141	2	1.371	0.87	0.05	1.13	0.69					4	0.000	0.78	0.06	2.05	0.50	1.99	0.73		
142	2	0.006	0.34	0.02	1.25	0.03					2	2.272	0.85	0.08	0.33	0.41				
143	4	0.000	0.74	0.06	0.78	0.16	2.31	1.14			4	0.000	0.87	0.06	0.24	0.41	1.25	0.58		
144	4	0.000	0.51	0.08	1.42	0.13	3.34	1.15			4	0.000	0.59	0.13	0.88	0.32	1.93	0.83		
145	2	1.750	0.77	0.04	0.72	0.22					4	0.000	0.79	0.13	0.46	0.46	1.78	1.00		
146	2	1.303	0.57	0.03	1.07	0.06														
147	2	0.476	0.49	0.02	1.11	0.05					2	1.334	0.40	0.05	1.19	0.10				
148	5	0.000	0.37	0.03	1.15	0.04					2	1.462	0.33	0.05	0.97	0.06				
149																				
150																				
151	5	0.000	0.24	0.01	1.06	0.02			0.81	0.01	5	0.000	0.16	0.01	0.96	0.01			0.85	0.02
152																				
153	5	0.000	0.11	0.02	0.90	0.01			0.79	0.01	5	0.000	0.10	0.01	0.68	0.01			0.93	0.02
154	5	0.000	0.09	0.01	0.74	0.01			0.91	0.02	2	3.324	0.27	0.06	0.53	0.14			1.00	0.00
155	5	0.000	0.07	0.00	0.61	0.00			0.85	0.02	5	0.000	0.12	0.01	0.37	0.01			0.78	0.02
156	5	0.000	0.04	0.00	0.57	0.00			0.55	0.01	6(5)	479.330	0.00	0.01	0.33	0.01			0.33	0.01

[a]: Modelfree parameters derived from backbone ^{15}N relaxation parameters tabulated in Table S1 using the program TENSOR2 and anisotropic rotational diffusion tensor model determined from a reduced group of 26 residues with relaxation parameters satisfying NOE $\geq$ 0.65 and $|T_1/\langle T_1\rangle - T_2/\langle T_2\rangle| \leq 1.5$ SD) at both 283 and 298 K.

[b]: Five combinations of *Modelfree* parameters were used in the fitting with Model-1(S^2), Model-2 (S^2 and τ_i), Model-3 (S^2 and R_{ex}), Model-4 (S^2, τ_i, and R_{ex}), and Model-5(S_s^2, S_f^2, and τ_i)). Model 6 indicates *Modlefree* fitting was unsatisfactory.

Table S3 Dynamics parameters for mIL-3_{33-156} resulting from *Modelfree* analysis (anisotropic model - II) [a]

	283 K										298K									
No	**Model[b]**	**χ^2**	**S_f^2**	**ΔS_f^2**	**τ_i**	**$\Delta\tau_i$**	**R_{ex}**	**ΔR_{ex}**	**S_s^2**	**ΔS_s^2**	**Model[b]**	**χ^2**	**S_f^2**	**ΔS_f^2**	**τ_i**	**$\Delta\tau_i$**	**R_{ex}**	**ΔR_{ex}**	**S_s^2**	**ΔS_s^2**
					(ns)		**(s^{-1})**								**(ns)**		**(s^{-1})**			
33	5	0.000	0.10	0.01	0.93	0.01			0.92	0.02	5	0.000	0.04	0.02	0.85	0.03			1.11	0.04
34	2	1.159	0.23	0.01	0.97	0.01					5	0.000	0.31	0.03	0.76	0.05			0.88	0.04
35	2	0.004	0.24	0.03	1.24	0.03														
36	2	1.996	0.21	0.01	1.19	0.03					2	1.624	0.20	0.03	0.93	0.07				
37	5	0.000	0.30	0.03	1.16	0.04			0.92	0.03	2	0.110	0.24	0.03	1.07	0.05				
38	2	2.410	0.47	0.02	1.10	0.04					2	0.786	0.46	0.05	0.82	0.08				
39	2	3.113	0.44	0.03	1.14	0.05					2	1.942	0.49	0.05	0.89	0.11				
40	2	1.840	0.56	0.02	1.24	0.05					2	2.606	0.61	0.05	0.92	0.12				
41	2	2.666	0.58	0.04	1.32	0.20					2	0.097	0.77	0.10	0.50	0.36				
42																				
43	5	0.000	0.81	0.07	2.30	2.49			0.87	0.06	1	2.615	0.97	0.05						
44	4	0.000	0.89	0.05	0.06	0.20	5.05	1.31			1	2.510	1.00	0.04						
45	1	4.762	0.97	0.05							1	2.983	1.00	0.13						
46	6(4)	3.432	0.84	0.09	10.77	4.30	3.62	1.79			2	1.311	0.95	0.03	0.20	0.51				
47	3	0.611	0.67	0.05			7.52	1.61			1	2.220	0.86	0.04						
48	1	6.088	1.00	0.05							4	0.000	0.79	0.08	1.43	0.48	3.67	0.73		
49	4	0.000	0.74	0.09	1.96	0.72	4.43	1.55			1	5.753	1.00	0.03						
50	6(3)	4.955	0.86	0.08			7.12	1.79			3	0.229	0.80	0.06			2.14	0.78		
51	3	0.078	0.90	0.08			11.45	2.31			4	0.000	0.61	0.07	2.55	0.68	5.27	0.61		
52	1	4.786	0.93	0.05							3	0.111	0.98	0.05			3.75	1.15		
53	1	3.518	1.00	0.04							4	0.000	0.83	0.06	1.63	0.53	2.10	0.48		
54	4	0.000	0.89	0.06	2.81	3.86	11.81	4.66			4	0.000	0.77	0.07	2.05	0.55	4.83	0.70		
55																				
56	2	0.001	0.78	0.04	2.06	1.20					5	0.000	0.84	0.03	0.93	0.27			0.91	0.03
57																				
58	2	2.825	0.63	0.03	1.69	0.29					2	2.224	0.67	0.03	0.74	0.08				
59	2	2.479	0.77	0.04	0.80	0.14					4	0.000	0.60	0.04	1.46	0.11	1.96	0.50		
60	4	0.000	0.74	0.04	0.79	0.12	2.63	0.76			2	0.609	0.56	0.03	0.83	0.07				
61	4	0.000	0.71	0.08	0.86	0.22	3.74	0.89			2	2.071	0.71	0.03	0.61	0.15				
62	4	0.000	0.58	0.04	1.39	0.09	1.76	0.51			2	0.000	0.74	0.06	0.85	0.33				
63																				

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64																				
65	2	2.175	0.69	0.03	1.55	0.29					2	0.543	0.59	0.06	1.14	0.19				
66																				
67	4	0.000	0.93	0.03	0.18	0.35	5.40	1.42			6(4)	0.118	0.00	0.16	1.49	0.26	12.02	2.20		
68	1	3.813	1.00	0.08																
69	4	0.000	0.81	0.09	1.32	1.35	10.58	3.19												
70	1	5.393	1.00	0.06																
71	4	0.000	0.80	0.16	2.85	4.33	20.40	7.56												
72	6(4)	0.379	0.84	0.06	10.77	4.17	4.57	2.13												
73	1	3.833	1.00	0.05																
74	6(5)	2.143	0.60	0.19	10.77	4.00			1.18	0.09										
75	3	2.615	1.00	0.08			5.59	2.69												
76	1	4.076	1.00	0.12																
77	1	4.347	1.00	0.06							4	0.000	0.85	0.06	2.62	1.68	1.72	0.53		
78	3	1.155	1.00	0.08			8.21	3.13			1	4.873	0.97	0.04						
79	6(4)	8.977	0.64	0.17	10.77	3.90	5.23	1.88			2	1.916	0.85	0.12	0.32	0.60				
80	4	0.000	0.67	0.16	4.79	3.64	3.04	1.31			4	0.000	0.72	0.05	0.05	0.02	4.37	0.65		
81	4	0.000	0.76	0.08	2.96	2.15	3.64	0.98												
82	1	5.029	0.84	0.06																
83	1	4.789	1.00	0.04							4	0.000	0.81	0.05	2.08	0.65	2.30	0.54		
84	3	1.128	0.92	0.08			6.74	1.70			4	0.000	0.78	0.12	1.28	0.80	5.48	1.45		
85	2	1.219	0.57	0.09	10.25	3.37														
86	4	0.000	0.71	0.08	1.25	0.32	5.18	1.55			3	0.197	0.91	0.10			6.52	2.06		
87	3	3.338	1.00	0.03			2.12	0.93			4	0.000	0.93	0.04	0.28	0.46	1.70	0.52		
88	4	0.000	0.69	0.09	0.02	0.02	8.23	1.99			4	0.000	0.64	0.09	0.03	0.02	8.59	1.37		
89	1	4.990	1.00	0.02							2	0.191	0.92	0.02	0.28	0.26				
90																				
91	4	0.000	0.78	0.05	0.03	0.01	8.42	1.39			4	0.000	0.77	0.06	0.02	0.02	3.68	0.93		
92	1	3.386	0.93	0.06							1	2.111	0.97	0.02						
93	1	3.795	1.00	0.02							4	0.000	0.88	0.05	0.92	0.42	2.20	0.71		
94	1	7.904	1.00	0.06							1	2.321	0.95	0.03						
95	3	1.604	0.77	0.08			4.37	2.09			2	2.144	0.86	0.05	0.46	0.32				
96	4	0.000	0.45	0.19	1.78	0.56	8.73	3.16			3	1.220	0.86	0.10			5.28	1.81		
97	1	2.939	1.00	0.05							4	0.000	0.32	0.11	2.46	0.76	10.27	1.78		
98	4	0.000	0.84	0.12	6.76	4.11	5.03	1.35			4	0.000	0.88	0.05	0.95	0.55	1.77	0.67		

99	3	0.252	0.70	0.05			5.69	1.47			2	0.486	0.87	0.03	7.35	2.11				
100	2	2.216	0.88	0.06	0.36	0.36					6(4)	0.019	0.00	0.27	3.97	2.25	16.00	3.80		
101	6(4)	1.648	0.22	0.23	10.77	3.66	13.05	2.48			1	4.850	1.00	0.10						
102	2	2.704	0.93	0.02	0.32	0.30					4	0.000	0.90	0.04	0.06	0.21	1.77	0.79		
103	1	5.193	1.00	0.05																
104	6(4)	0.199	0.76	0.13	10.77	4.08	4.54	1.69			6(4)	1.439	0.51	0.24	7.51	2.53	7.67	2.78		
105	4	0.000	0.73	0.09	0.03	0.05	5.32	1.76			4	0.000	0.75	0.10	1.64	0.58	4.09	0.82		
106	4	0.000	0.77	0.08	1.85	1.08	5.67	1.58			4	0.000	0.67	0.12	1.26	0.43	12.98	1.72		
107	1	1.411	1.00	0.04																
108																				
109	4	0.000	0.85	0.03	0.07	0.04	3.85	0.70			4	0.000	0.86	0.03	0.17	0.18	1.11	0.35		
110	2	0.040	0.86	0.05	1.31	0.62					2	0.794	0.64	0.03	1.10	0.12				
111	2	2.398	0.87	0.03	0.45	0.25														
112	4	0.000	0.52	0.07	1.50	0.13	2.68	1.00												
113	2	3.098	0.87	0.05	0.27	0.28					3	2.895	1.00	0.17			13.15	5.85		
114	4	0.000	0.58	0.07	1.46	0.17	7.78	1.40			4	0.000	0.44	0.21	1.40	0.45	11.72	2.50		
115	4	0.000	0.73	0.06	1.08	0.21	4.20	1.09			4	0.000	0.68	0.07	1.39	0.26	1.98	0.92		
116	4	0.000	0.77	0.05	0.05	0.03	3.66	0.99			4	0.000	0.69	0.04	0.05	0.01	1.57	0.51		
117																				
118	5	0.000	0.77	0.04	1.27	0.19			0.87	0.04	5	0.000	0.64	0.03	1.40	0.13	0.00	0.00	0.93	0.02
119	4	0.000	0.86	0.06	0.11	0.23	4.06	1.38	1.00	0.00	1	1.823	1.00	0.04						
120	2	0.265	0.94	0.04	0.27	0.40					1	4.861	0.97	0.05						
121	2	2.139	0.93	0.04	0.31	0.40					4	0.000	0.95	0.03	0.17	0.53	1.13	0.47		
122	3	0.756	0.87	0.10			8.16	2.36			1	5.369	1.00	0.04						
123	4	0.000	0.89	0.06	0.09	0.37	2.57	1.16			4	0.000	0.78	0.07	1.64	0.45	2.08	0.50		
124	2	1.994	0.87	0.08	1.28	1.39	0.00	0.00			1	4.629	1.00	0.02						
125	3	3.538	0.72	0.04			6.27	1.18			3	0.045	0.86	0.03			1.65	0.53		
126	6(5)	8.438	0.81	0.10	10.77	3.41	0.00	0.00	1.20	0.08	4	0.000	0.82	0.06	3.00	1.77	1.60	0.51		
127	4	0.000	0.75	0.07	0.04	0.03	8.61	2.40			4	0.000	0.84	0.05	0.07	0.20	3.13	0.88		
128	3	2.310	1.00	0.05			6.15	2.33			4	0.000	0.88	0.06	0.05	0.25	2.34	0.68		
129	6(4)	0.360	0.54	0.16	10.77	3.69	7.86	1.54			4	0.000	0.85	0.07	0.96	0.50	1.77	0.73		
130	3	1.170	0.92	0.06			4.78	1.48			1	1.604	1.00	0.02						
131	3	0.119	0.79	0.01			7.31	1.27			1	1.662	1.00	0.02						
132	2	5.436	0.80	0.08	4.97	3.49					1	6.547	1.00	0.02						
133	4	0.000	0.65	0.15	2.47	2.56	6.13	2.00			3	1.550	0.86	0.08			3.22	1.22		

134	1	0.004	0.87	0.14																
135	3	2.725	0.86	0.12			13.54	4.10												
136	3	0.560	0.73	0.06			11.97	2.32			4	0.000	0.82	0.06	0.04	0.04	5.85	0.93		
137	3	2.288	1.00	0.05			3.36	2.37												
138	6(5)	0.003	0.75	0.10	10.77	3.20			1.31	0.11	4	0.000	0.00	0.32	2.76	1.70	11.44	2.58		
139	4	0.000	0.76	0.06	1.07	0.22	6.03	1.20			1	1.598	0.95	0.06						
140	4	0.000	0.60	0.12	1.36	0.34	7.75	1.86			4	0.000	0.61	0.17	1.20	0.49	4.52	1.70		
141	1	3.554	0.96	0.04							4	0.000	0.79	0.06	1.92	0.46	2.39	0.69		
142	2	0.524	0.40	0.03	1.18	0.04					4	0.000	0.78	0.17	0.57	0.55	4.19	2.06		
143	4	0.000	0.80	0.05	0.54	0.21	2.79	0.92			2	3.496	0.89	0.03	0.34	0.27				
144	4	0.000	0.51	0.08	1.44	0.12	3.36	1.01			4	0.000	0.49	0.13	1.09	0.25	2.02	0.93		
145	2	2.279	0.82	0.04	0.51	0.24					2	2.863	0.83	0.05	0.35	0.32				
146	2	0.001	0.67	0.03	0.87	0.08														
147	2	0.365	0.49	0.02	1.12	0.05					2	1.596	0.42	0.05	1.15	0.11				
148	5	0.000	0.37	0.03	1.15	0.04			0.90	0.03	2	1.340	0.30	0.04	1.02	0.05				
149																				
150																				
151	5	0.000	0.24	0.01	1.07	0.02			0.81	0.01	5	0.000	0.15	0.01	0.97	0.01			0.85	0.02
152																				
153	5	0.000	0.11	0.02	0.90	0.01			0.79	0.01	5	0.000	0.10	0.01	0.68	0.01			0.93	0.02
154	5	0.000	0.12	0.01	0.71	0.01			0.91	0.02	2	3.389	0.31	0.06	0.46	0.15				
155	5	0.000	0.07	0.00	0.61	0.00			0.85	0.02	5	0.000	0.14	0.01	0.33	0.02			0.79	0.03

[a]: Similar as Table S2 except rotational diffusion tensor parameters determined from the original group of residues (51 and 37 residues at 283 and 298 K, respectively, that satisfy both NOE $\geq$ 0.65 and $|T_1/\langle T_1\rangle - T_2/\langle T_2\rangle| \leq 1.5$ SD) were used.

[b]: Five combinations of *Modelfree* parameters were used in the fitting with Model-1(S^2), Model-2 (S^2 and τ_i), Model-3 (S^2 and R_{ex}), Model-4 (S^2, τ_i, and R_{ex}), and Model-5(S_s^2, S_f^2, and τ_i)). Model 6 indicates *Modlefree* fitting was unsatisfactory.

Table S4 Dynamics parameters for mIL-$3_{33\text{-}156}$ resulting from *Modelfree* analysis (isotropic model) [a]

	283K							298K						
NO	S^2	ΔS^2	$\tau_{f,s}$	$\Delta\tau_{f,s}$	*R*ex (s^{-1})	Δ*R*ex (s^{-1})	model[b]	S^2	ΔS^2	$\tau_{f,s}$	$\Delta\tau_{f,s}$	*R*ex (s^{-1})	Δ*R*ex (s^{-1})	model[b]
33	0.09	0.01	920.47	7.66			5	0.05	0.00	843.08	0.00			5(-)
34	0.25	0.02	929.74	14.20			5	0.27	0.03	727.05	46.49			5
35	0.24	0.03	1217.68	34.97			5							
36	0.25	0.02	1130.80	27.08			5	0.23	0.01	881.10	0.00			5(-)
37	0.25	0.03	1166.46	32.84			5	0.22	0.03	1059.95	49.20			5
38	0.44	0.01	1117.31	0.00			5(-)	0.43	0.06	820.57	83.42			5
39	0.49	0.05	984.75	70.12			5	0.54	0.02	756.36	0.00			5(-)
40	0.62	0.03	1047.33	69.11			5	0.74	0.08	526.32	239.71			5(-)
41	0.65	0.06	1319.28	368.65			5	0.78	0.03	273.69	421.99			2
42														
43	0.80	0.07	1380.75	820.44			5	0.92	0.09	400.00	1566.99			2
44	0.76	0.05	28.99	12.58	8.90	1.24	4	0.80	0.11			4.61	1.72	3
45	0.75	0.07	26.31	17.55	8.09	2.57	4	1.00	0.21					1
46	0.99	0.08			4.25	1.81	3	0.87	0.04	61.01	28.19	1.46	0.64	4
47	0.60	0.04			9.37	1.57	3	0.74	0.05			2.35	0.82	3
48	0.92	0.10			8.19	2.63	3	0.90	0.05	147.37	138.68	3.16	0.74	4(-)
49	1.00	0.00			2.56	0.00	3(-)	1.00	0.05					1
50	0.75	0.07			10.34	1.54	3(-)	0.75	0.05			2.77	0.72	3
51	0.79	0.07			14.83	2.14	3	0.94	0.02	400.00	0.39	3.35	0.35	4(-)
52	0.74	0.06			6.81	1.74	3	0.91	0.07			4.93	1.12	3
53	0.95	0.08			4.44	1.81	3	0.95	0.03	357.90	1123.95	1.05	0.38	4(-)
54	1.00	0.00			11.40	0.00	3(-)	0.95	0.05	400.00	1330.49	4.21	0.64	4(-)
55														
56	0.88	0.03	1366.69	0.00			5(-)	0.75	0.04	921.67	221.17			5
57														
58	0.73	0.02	1311.94	0.00			5(-)	0.67	0.01	693.60	0.00			5(-)
59	0.79	0.05	472.48	223.41	0.00	0.00	5	0.76	0.01	966.68	0.00			5(-)
60	0.82	0.03	397.97	192.28	2.69	0.67	4	0.58	0.01	737.95	0.00			5(-)
61	0.84	0.05	400.00	396.04	1.05	0.76	4(-)	0.69	0.01	662.87	0.00			5(-)
62	0.68	0.01	1168.48	0.00	0.00	0.00	5(-)	0.70	0.08	924.70	260.01			5
63														
64														
65	0.83	0.06	916.91	329.58	0.00	0.00	5	0.65	0.08	880.19	224.48			5
66														
67	0.87	0.05	87.50	48.94	6.52	1.43	4	0.74	0.24	400.00	1094.07	6.32	2.63	4(-)

68	0.96	0.12					1							
69	0.99	0.13			10.32	3.50	3							
70	1.00	0.09					1							
71	1.00	0.00			20.00	0.00	3							
72	1.00	0.05					1(-)							
73	1.00	0.08					1							
74	1.00	0.00					3(-)							
75	1.00	0.00			7.71	0.00	3							
76	1.00	0.21					1							
77	1.00	0.10					1	0.97	0.02	400.00	0.39	0.60	0.38	4(-)
78	1.00	0.00			9.58	0.00	3	0.95	0.06					1
79	1.00	0.00			3.51	0.00	3(-)	0.84	0.09	327.54	1198.73			2
80	1.00	0.00			0.25	0.00	3(-)	0.71	0.05	48.03	13.50	4.32	0.72	4
81	1.00	0.00			0.97	0.00	3(-)							
82	0.72	0.07			7.92	3.09	3							
83	1.00	0.07					1	0.95	0.02	400.00	0.45	1.27	0.44	4(-)
84	0.87	0.09			7.50	1.62	3	0.90	0.11	400.00	1433.91	4.21	1.44	4(-)
85	1.00	0.00					1(-)							
86	0.90	0.07	378.95	831.08	4.21	1.39	4(-)	0.86	0.11	0.00	0.00	7.20	1.99	3
87	0.93	0.04			5.28	0.85	3	0.90	0.05	149.27	138.63	1.77	0.70	4
88	0.64	0.07	21.65	10.05	9.50	1.98	4	0.59	0.09	31.00	13.93	9.28	1.21	4
89	0.94	0.04			3.76	0.98	3	0.86	0.04	95.64	36.14	1.13	0.58	4
90														
91	0.64	0.04	17.25	6.53	12.70	1.29	4(-)	0.70	0.05	19.22	9.43	4.90	0.83	4
92	0.93	0.07					1	0.96	0.03					1(-)
93	1.00	0.04					1(-)	0.91	0.03	155.77	98.50	2.23	0.69	4
94	0.74	0.10	35.58	23.75	11.26	3.30	4	0.94	0.03					1
95	0.85	0.07					1(-)	0.84	0.06	400.00	520.48			2
96	1.00	0.00			3.46	0.00	3(-)	0.76	0.10			7.06	1.76	3
97	1.00	0.10					1	0.91	0.03	400.00	1.59	6.21	1.57	4(-)
98	1.00	0.00			4.83	0.00	3	0.95	0.06	526.32	1024.98			5(-)
99	0.61	0.04			8.20	1.34	3	0.95	0.41	10000.00	125786.85			5(-)
100	0.84	0.07	168.42	162.12	0.00	0.00	2(-)	1.00	0.00			9.63	0.00	3
101	1.00	0.00			8.30	0.00	3	1.00	0.18					1
102	0.82	0.04	64.18	22.53	5.08	1.19	4	0.85	0.04	44.88	21.66	2.27	0.76	4
103	0.82	0.09			11.75	4.04	3							
104	1.00	0.00			3.26	0.00	3	1.00	0.43	0.00	0.00	5.26	0.00	4(-)
105	0.64	0.08	21.65	8.74	8.06	1.45	4(-)	0.90	0.06	147.37	163.34	3.16	0.88	4(-)
106	0.95	0.08	400.00	1968.59	5.26	1.51	4	0.86	0.04	400.00	1.42	11.72	1.40	4(-)
107	1.00	0.08					1							

108														
109	0.83	0.04	65.20	19.73	3.81	0.73	4	0.88	0.01	249.94	160.88			2
110	0.95	0.02	273.68	1004.17	0.00	0.00	2	0.72	0.02	779.84	0.00			5(-)
111	0.90	0.02	315.79	535.16			2							
112	0.86	0.02	400.00	135.52			2(-)							
113	0.84	0.05	168.42	128.29			2	1.00	0.00			14.80	0.00	3
114	0.90	0.04	357.90	713.31			2(-)	0.79	0.20	400.00	1173.08	9.47	2.35	4(-)
115	0.90	0.03	357.90	516.74			2(-)	0.76	0.03	1159.80	0.00			5(-)
116	0.88	0.04	104.62	52.84			2	0.74	0.02	71.89	12.27			2
117														
118	0.82	0.04	76.53	23.37			2	0.61	0.03	1258.36	119.12			5
119	0.80	0.07	71.56	36.84	5.35	1.50	4	1.00	0.07					1
120	0.78	0.06	46.93	21.89	5.25	1.64	4	0.78	0.09	47.15	33.13	3.34	1.53	4
121	0.82	0.07	61.90	33.53	5.87	2.01	4	0.87	0.04	59.57	29.38	2.26	0.58	4
122	0.86	0.11			7.74	2.38	3	0.95	0.09	400.00	2617.32			2
123	0.95	0.02	294.74	1319.50			2	0.95	0.04	378.95	1234.92	0.00	0.39	4(-)
124	0.95	0.08	400.00	1989.29			2	0.96	0.04	400.00	1162.07			2
125	0.66	0.04	11.07	5.63	7.48	1.21	4	0.83	0.03			1.77	0.53	3
126	1.00	0.44	0.00	0.00	1.05	0.00	4(-)	0.97	0.02	400.00	0.39	0.60	0.38	4(-)
127	0.75	0.07	44.62	22.78	8.30	2.49	4	0.82	0.06	66.32	32.95	3.04	0.92	4
128	0.95	0.08			8.18	2.21	3	0.84	0.06	39.34	23.05	2.78	0.77	4
129	1.00	0.00			5.40	0.00	3(-)	0.89	0.05	172.72	181.19	1.82	0.75	4
130	0.89	0.06			5.23	1.44	3	0.97	0.03					1
131	0.74	0.01			8.60	1.30	3	0.98	0.03					1
132	1.00	0.00			1.19	0.00	3(-)	1.00	0.03					1(-)
133	1.00	0.00			3.18	0.00	3(-)	0.79	0.07			4.49	1.09	3
134	0.83	0.16					1							
135	0.73	0.11	26.39	20.01	16.86	4.18	4							
136	0.63	0.05			14.72	2.43	3	0.76	0.06	31.53	14.76	6.75	0.88	4
137	1.00	0.00			5.31	0.00	3							
138	1.00	0.00			2.93	0.00	3(-)	0.90	0.51	400.00	6813.78	5.26	4.17	4(-)
139	0.88	0.02	400.00	1.01	6.43	1.01	4(-)	0.93	0.07					1
140	0.90	0.08	400.00	906.82			2(-)	0.84	0.13	400.00	1029.22	2.11	1.70	4(-)
141	0.92	0.05					1	0.95	0.05	400.00	1165.57	1.05	0.66	4(-)
142	0.47	0.01	1045.07	0.00			5(-)	0.80	0.13	196.76	390.34	4.55	2.10	4
143	0.84	0.01	394.46	0.00			5(-)	0.90	0.02	315.79	623.51			2
144	0.66	0.01	1157.11	0.00			5(-)	0.67	0.01	719.72	0.00			5(-)
145	0.76	0.02	716.94	0.00			5(-)	0.81	0.06	400.00	459.91			2
146	0.72	0.04	684.72	94.33			5							
147	0.55	0.03	985.12	53.46			5	0.47	0.02	1024.18	0.00			5(-)

148	0.31	0.03	1151.91	40.52	5	0.28	0.05	1000.19	53.95	5
149										
150										
151	0.19	0.01	1051.83	19.98	5	0.13	0.01	944.74	13.15	5
152										
153	0.09	0.02	877.98	14.24	5	0.10	0.01	659.90	11.26	5
154	0.11	0.01	695.35	6.92	5	0.30	0.01	463.34	0.00	5(-)
155	0.07	0.01	583.77	4.26	5	0.13	0.01	288.29	21.51	5
156	0.02	0.00	556.84	3.68	5					

[a]: ^{15}N R_1, R_2 and steady-state ^{15}N-{^{1}H} NOE fitted with an isotropic approximation for the overall rotational correlation using the *Modelfree* program (Art Palmer, Columbia University). One of five combinations of *Modelfree* parameters, similar to the model selection approach (Mandel, A. M., Akke, M., and Palmer, A. G. (1995) *J. Mol. Biol.* 246, 144-163), with an N-H bond length of 1.02 Å and a chemical shift anisotropy of -170 ppm for ^{15}N nuclei were used for the analysis. For the analysis performed in the *Modelfree* program, the best combination of fitting parameters for each individual backbone amide (Model-1: S^2, Model-2: S^2 and τ_e, Model-3: S^2 and R_{ex}) was determined with a 90% fitting confidence for 500 randomly distributed back-calculated relaxation parameters, except for models Model-4 (S^2, τ_e, and R_{ex}) and Model-5 (S_s^2, S_f^2, and τ_e) where fittings are only considered satisfactory when the square mean error between back-calculated and experimentally obtained relaxation parameters is nil. For the original *Modelfree* formula, the limit of the effective internal correlation was set at 400 ps, whereas for the extended *Modelfree* formula the limit of the effective internal correlation was set to 10 ns. The limit of conformational exchange, R_{ex}, was set to 20 s^{-1}.

[b]: The minus sign in parentheses indicates that the particular residue did not fit the model satisfactorily. Comparing with *Modelfree* analysis using an anisotropic rotational diffusion tensor model, only two-thirds of residues could be fitted satisfactorily to one of five *Modelfree* parameters combinations. Distribution of fitted backbone amides among the five models are 12 (S^2), 8 (S^2 and τ_e), 23 (S^2 and R_{ex}), 14 (S^2, τ_e, and R_{ex}), and 20 (S^2_f, S^2_s, and τ_e), respectively for 283 K. Corresponding numbers resulting from the analysis of ^{15}N relaxation parameters measured at 298 K are 9 (S^2), 11 (S^2 and τ_e), 10 (S^2 and R_{ex}), 14 (S^2, τ_e, and R_{ex}), and 11 (S^2_f, S^2_s, and τ_e), respectively.

Table S5 Conformational exchange parameters of mIL-$3_{33\text{-}156}$ residues at 298 K as detected from ^{15}N relaxation dispersion [a]

Residues	τ_{ex} (ms)	$\Phi_{ex}\,\tau_{ex}$ (s^{-1})	R_2^{ave} (s^{-1})
Glu49	1.22 ± 0.29	12.8 ± 2.8	22.6 ± 0.5
Lys60	0.59 ± 0.15	21.0 ± 3.4	21.8 ± 1.2
Leu68	0.55 ± 0.08	46.8 ± 4.2	21.3 ±1.6
Asn70	1.05 ± 0.01	79.0 ± 4.5	22.1 ± 0.7
Arg74	0.82 ± 0.09	45.1 ± 3.8	22.5 ± 0.9
Val76	1.00 ± 0.10	36.2 ± 3.0	21.8 ± 0.5
Ser79	0.74 ± 0.15	46.9 ± 6.6	20.6 ± 1.8
Lys80	0.98 ± 0.15	25.4 ± 3.1	17.9 ± 0.6
Gln101	0.88 ± 0.12	56.7 ± 5.8	22.3 ± 1.2
Lys102	0.91 ± 0.11	22.9 ± 2.2	15.3 ±0.4
Cys106	0.62 ± 0.09	48.5 ± 4.8	18.2 ± 1.6
Leu107	0.91 ± 0.20	36.1 ± 6.1	23.3 ± 1.3
Asn112	0.74 ± 0.12	21.0 ± 2.5	16.1 ± 0.7
Asp113	1.03 ± 0.09	31.1 ± 2.2	17.5 ± 0.4
Ser114	0.49 ± 0.10	21.5 ± 2.3	17.5 ± 0.4
Ala115	0.58 ± 0.15	17.0 ± 2.7	13.4 ± 1.0
Val119	1.17 ± 0.30	28.7 ± 6.1	22.2 ± 0.8
Met135	1.27 ± 0.25	25.9 ± 4.5	21.3 ± 0.5
His137	1.42 ± 0.41	57.4 ± 15.2	25.0 ± 1.4
Leu138	0.86 ± 0.13	48.8 ± 5.4	22.5 ± 1.2
Asp140	1.10 ± 0.26	21.3 ± 4.2	21.7 ± 0.6
Thr143	1.04 ± 0.20	16.4 ± 2.6	14.8 ± 0.4
Leu145	0.70 ± 0.14	21.7 ± 2.8	12.7 ± 0.8

[a]: See *Material and Methods* for details of fitting.