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Supporting Information

Structure of Monomeric Transthyretin Carrying the Clinically Important T119M Mutation

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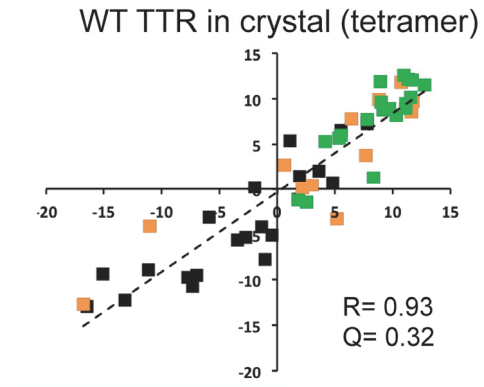

Figure S1. Comparison of experimental ^{1}H-^{15}N dipolar couplings measured in T119M M-TTR (x-axis) with those back-calculated from the monomeric subunit of the tetrameric crystal structure of wild-type TTR (y-axis; PDB id: 1F41;[1] Resolution = 1.5 Å). RDCs of residues in the D/A/G/H-sheet are colored in orange, those in the C/B/E/F-sheet in green.

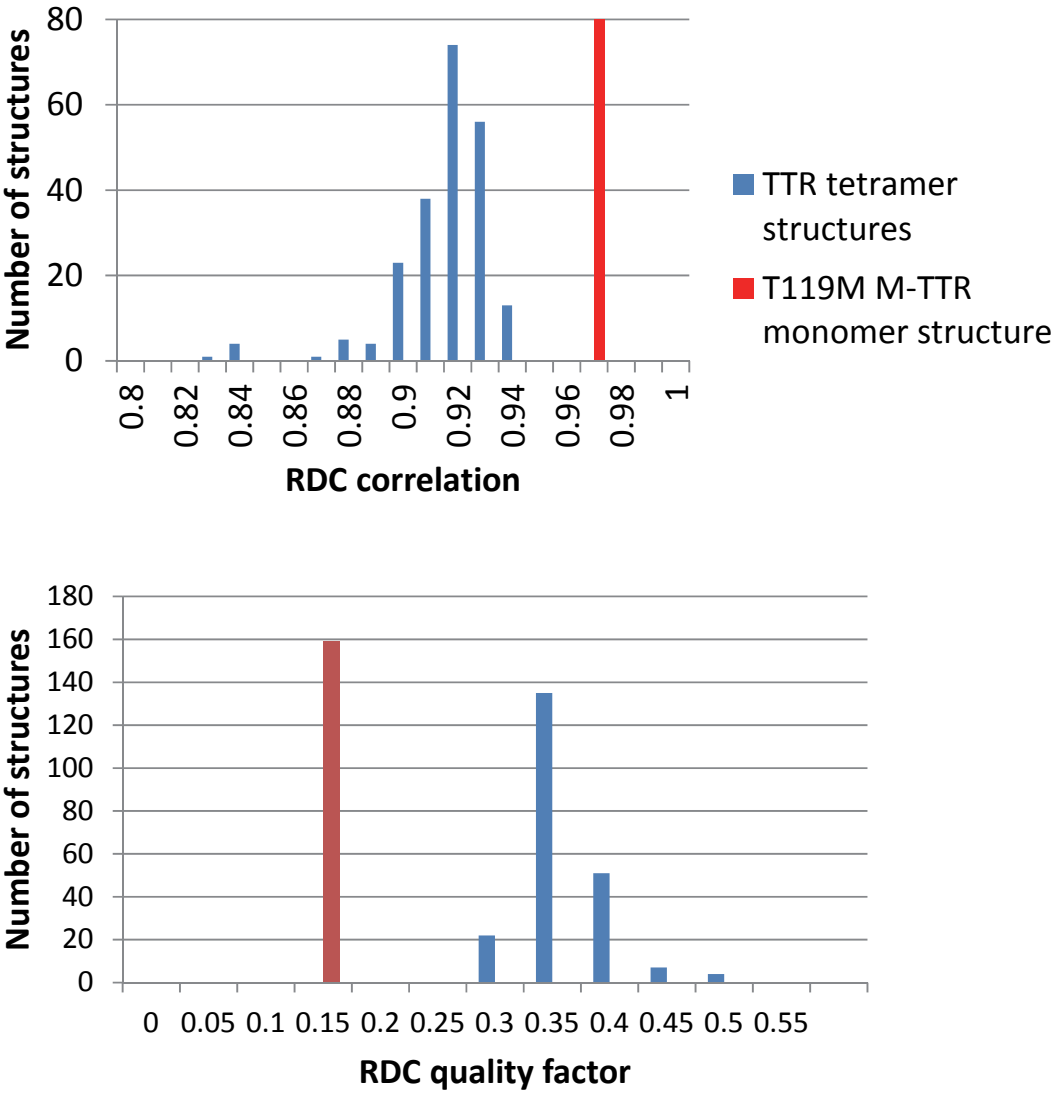

Figure S2. Comparison of experimental ^{1}H-^{15}N RDCs, which were measured for T119M M-TTR, and values back-calculated from 219 tetramer structures (blue bars) deposited in the ProteinDataBank (please see Table S3 for PDB ids). Upper panel: Pearson's correlation coefficients. Most structures have correlation coefficients of 0.91 to 0.93. Lower panel: dipolar coupling quality factors with most crystal structures having values between 0.30 and 0.40. A fit of the experimental ^{1}H-^{15}N RDCs, which were not used in the structure calculation of T119M M-TTR, to the 3D structure of T119M M-TTR (determined in the current study), results in a Pearson's correlation coefficient of 0.97 and a RDC quality factor of 0.196 (marked as red bars in panels a and b, respectively).

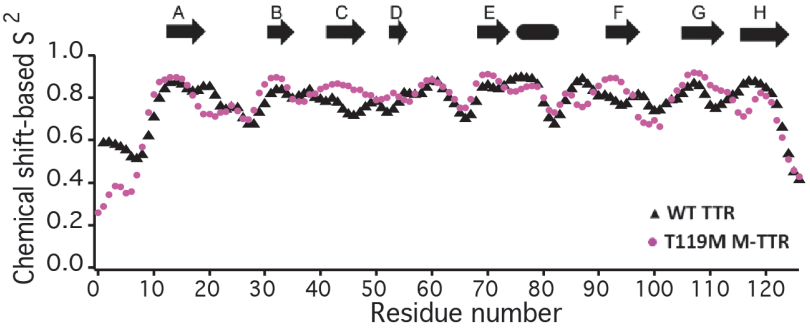

Figure S3. S^2 backbone order parameters predicted from experimental chemical shifts of T119M M-TTR (purple) and wild-type TTR (black; BMRB id 5507)[2] using TALOS-N.[3] The location of secondary structure elements in wild-type TTR is shown above.

Table S1. NMR constraints and structural statistics for the ensemble of 20 lowest-energy structures of T119M M-TTR.

distance constraints	2238
- intraresidue ($i = j$)	493
- sequential ($i - j = 1$)	665
- medium range ($1 < (i - j) \leq 5$)	254
- long range ($i - j > 5$)	826
dihedral angle constraints	214
- φ	93
- ψ	97
- χ_1	24
number of constraints per residue	19.3
number of long-range constraints per residue	6.5
CYANA target function (Å)	1.29 (± 0.06)
average number of distance constraints violations per conformer (> 0.5 Å)	0
average number of dihedral angle constraints violations per conformer	0
average r.m.s.d. for ordered residues[a] to the mean structure (Å)	
- backbone atoms (N, Cα, C')	0.5
- all atoms	0.8
Ramachandran plot summary for ordered residues[a] from PROCHECK	
- most favored regions (%)	84.8
- additionally allowed regions (%)	15.2
- generously allowed regions (%)	0.0
- disallowed regions (%)	0.0
PROCHECK raw score[a] (φ and ψ/all dihedral angle)	-0.67/-0.68
PROCHECK z-score[a] (φ and ψ/all dihedral angle)	-2.32/-4.02

[a] Residues 10−97, 105−115, and 117−126 of T119M M-TTR were considered ordered by the Protein Structure Validation Software Suite.

Table S2. NOE contacts to M119 observed in 3D NOESY-HSQC spectra of T119M M-TTR.

118	THR	QG2	119	MET	H
107	ILE	QD1	119	MET	QE
118	THR	HB	119	MET	HA
119	MET	HA	119	MET	QE
93	VAL	HB	119	MET	QE
107	ILE	HG13	119	MET	QE
109	ALA	HA	119	MET	HB2
119	MET	QE	120	ALA	H
93	VAL	H	119	MET	QE
94	VAL	H	119	MET	QE
109	ALA	HA	119	MET	QE
93	VAL	HA	119	MET	QE
118	THR	HB	119	MET	HB2
109	ALA	QB	119	MET	QE
93	VAL	QG1	119	MET	QE
93	VAL	QG2	119	MET	QE
107	ILE	QG2	119	MET	QE
73	ILE	QD1	119	MET	QE
71	VAL	H	119	MET	QE
118	THR	HA	119	MET	H
109	ALA	HA	119	MET	H
119	MET	H	119	MET	HB2
118	THR	H	119	MET	HB2
119	MET	H	120	ALA	H
119	MET	HB3	120	ALA	H
119	MET	HB2	120	ALA	H

Table S3. PDB ids of TTR structures, which were compared to ^{1}H-^{15}N RDCs that were measured for T119M M-TTR (see Figure S2).

	4ydn	3gs7	5al0
1tsh	1thc	4pwi	3cbr
1e3f	2b16	4tqi	1ijn
1dvs	3ipe	2gab	2qgd
2try	3nee	3cft	4wnj
1bz8	1etb	3u2i	2f7i
1iii	3fcb	4n85	4iki
1dvy	3hj0	3eso	3imw
1dvz	4ik7	3ims	3ng5
1dvq	4tl4	4wns	4tls
1dvx	1eta	1sok	3a4e
3i9i	2b15	3p3r	3p3s
2g3z	4ank	4hjt	3p3u
4tm9	4ikj	4pwf	4ac2
1tyr	3bt0	3d2t	2fbr
1dvt	3djz	4act	4y9b
1iik	3esp	4pme	2g9k
4mas	4fi7	4tqp	4i89
2trh	4hju	3p3t	2qgb
1tlm	4tne	1qwh	3a4f
2g3x	3i9p	2noy	1fh2
4fi8	4n87	2qge	4y9c
4n86	1zd6	3esn	4ik6
2g5u	4hiq	3imr	4wo0
4ac4	1e4h	3cfm	2b77
1bzd	1ttc	3neo	4abv
1dvu	2b9a	4his	4pvm
3tfb	3cn3	3dk2	1soq
4tkw	3kgt	3cfq	4mrb
1tha	3w3b	4mrc	4pm1
1bmz	2b14	2h4e	2qel
1ttb	3u2j	4pvn	3cxf
4tlt	4y9g	4qxv	3gs4
1e5a	3nex	4y9e	2f8i
3kgu	4fi6	3glz	3d7p
4pwg	4ikl	3ipb	5al8
1f41	4ky2	4pvl	3a4d
3djs	3kgs	5boj	4y9f
1ttr	4pwk	1tta	1g1o
3imt	4qrf	2g4g	4iiz
3nes	1fhn	4pwe	5akv
2qgc	1tt6	1f86	4abq
1bm7	1zcr	4abw	4abu
1bze	3i9a	3cn4	4i85
3gs0	4tl5	4qya	3djt
4l1t	1y1d	4tlk	5akt
4ydm	3dk0	4pwj	2flm
3ozl	4pmf	5aks	1gko
4hjs	3cfn	3b56	3djr
1z7j	3cn2	4tqh	3ssg
1tz8	3imu	3cn1	3grg
3fc8	3imv	4ikk	3dgd
3m1o	3ozk	2g4e	3did
4tq8	4l1s	1u21	3grb
2roy	4pwh	3cn0	3gps

[1] A. Hornberg, T. Eneqvist, A. Olofsson, E. Lundgren, A. E. Sauer-Eriksson, *J Mol Biol* **2000**, *302*, 649-669.
[2] K. Liu, J. W. Kelly, D. E. Wemmer, *J Mol Biol* **2002**, *320*, 821-832.
[3] Y. Shen, A. Bax, *Methods Mol Biol* **2015**, *1260*, 17-32.