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**Sample-size estimation**

* You should state whether an appropriate sample size was computed when the study was being designed
* You should state the statistical method of sample size computation and any required assumptions
* If no explicit power analysis was used, you should describe how you decided what sample (replicate) size (number) to use

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Does not apply. No statistical method or power analysis was used.

**Replicates**

* You should report how often each experiment was performed
* You should include a definition of biological versus technical replication
* The data obtained should be provided and sufficient information should be provided to indicate the number of independent biological and/or technical replicates
* If you encountered any outliers, you should describe how these were handled
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* High-throughput sequence data should be uploaded before submission, with a private link for reviewers provided (these are available from both GEO and ArrayExpress)

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As most of the methods used in this manuscript are well established in our lab, the amount of replicates was chosen reasonable based on experience. Most experiments comprise a sample size of n = 3 and the values are shown as a mean with SD. Information on experiment replicated can be found in the figure legends or in the Materials and Methods section. Outliers or exclusion of data do not apply. The thermal stability recorded using CD spectroscopy were shown to be almost perfectly reproducible with invisible error bars, why we decided a single recording is sufficient. To still support the Tm values we chose GdmCl unfolding as an orthogonal method.

**Statistical reporting**

* Statistical analysis methods should be described and justified
* Raw data should be presented in figures whenever informative to do so (typically when N per group is less than 10)
* For each experiment, you should identify the statistical tests used, exact values of N, definitions of center, methods of multiple test correction, and dispersion and precision measures (e.g., mean, median, SD, SEM, confidence intervals; and, for the major substantive results, a measure of effect size (e.g., Pearson's r, Cohen's d)
* Report exact p-values wherever possible alongside the summary statistics and 95% confidence intervals. These should be reported for all key questions and not only when the p-value is less than 0.05.

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Most figures show data of a mean of n = 3 with SD as error bars or error bars depicted as background areas in case of a high amount of data points (fibril formation assays). Information on this can be found in the figure legend.

(For large datasets, or papers with a very large number of statistical tests, you may upload a single table file with tests, Ns, etc., with reference to sections in the manuscript.)

**Group allocation**

* Indicate how samples were allocated into experimental groups (in the case of clinical studies, please specify allocation to treatment method); if randomization was used, please also state if restricted randomization was applied
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* Include model definition files including the full list of parameters used
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The DNA sequence of the studied patient cDNA sequence was deposited in the GenBank under the accession number MK962887. Structure factors and coordinates of the solved crystal structures were deposited to the Protein Data Bank under the accession codes 6SM1 and 6SM2.