**SUPPORTING INFORMATION**

# Comparative study of the stabilities of synthetic *in vitro* and natural *ex vivo* transthyretin amyloid fibrils

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*Running title: Stability of natural and synthetic TTR amyloid fibrils*

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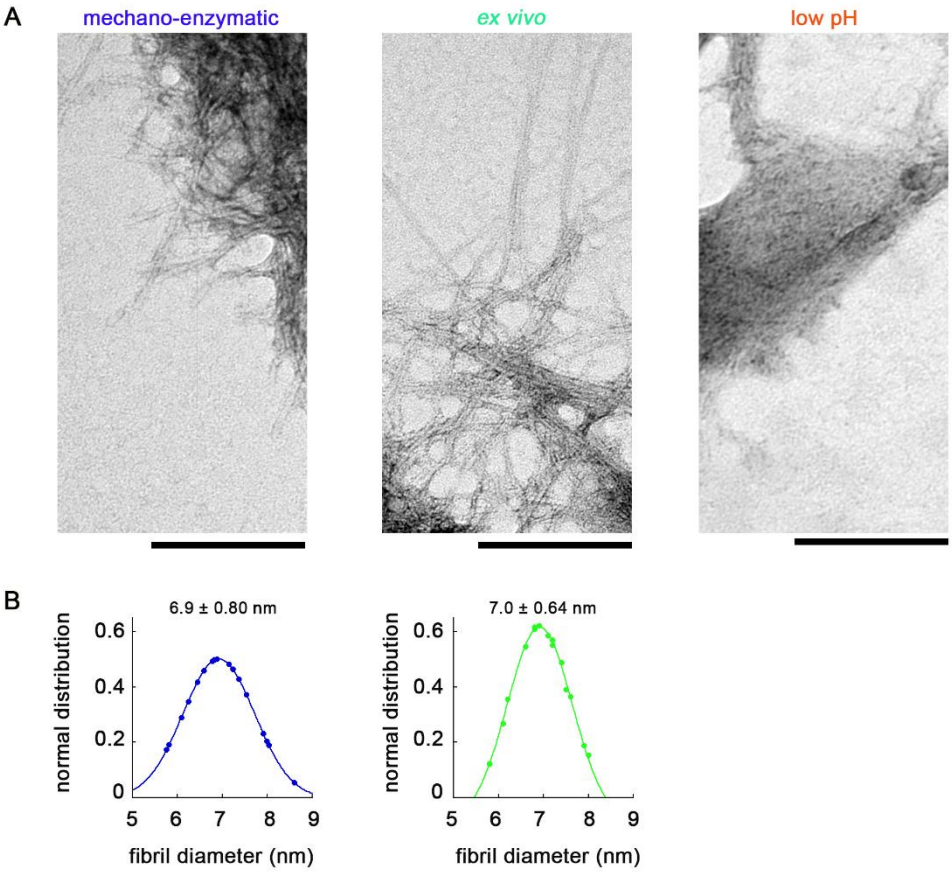


**Fig. S1. TEM images of fibrils.** *A*, additional electron micrographs of negatively stained TTR *in vitro* fibrils prepared with the mechano-enzymatic mechanism, at low pH or extracted from human amyloidotic tissue (scale bar, 200 nm). *B*, TEM images of both mechano-enzymatic and *ex vivo* fibrils were analyzed to assess fibril diameter using ImageJ software as described in Experimental Procedures. Measurements in each case are normally distributed with an average diameter of approximately 7 nm. Material generated at low pH could not be processed for this purpose.

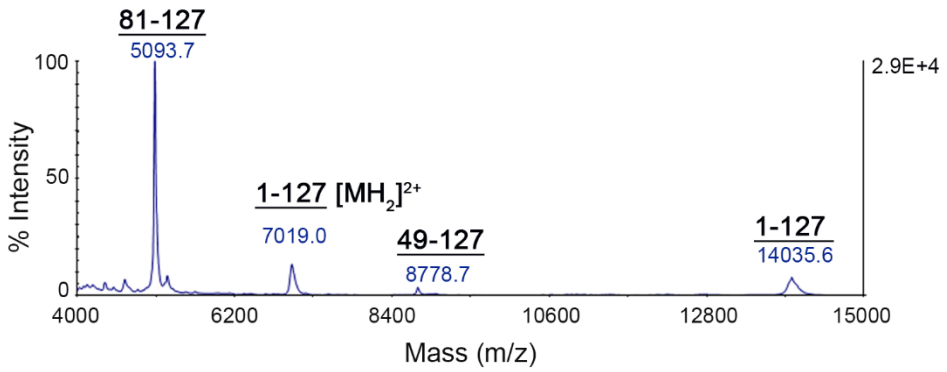


**Fig. S2. Main component in the recombinant V122I TTR mechano-enzymatic fibrils**. The pellet containing the fibrillar material was analysed in linear mode MALDI TOF as described in Experimental Procedures. Peaks at m/z of 5093.7 and 8778.7 are related to the +1 ions corresponding to the 81-127 and 49-127 fragments of recombinant V122I TTR respectively; peaks at m/z of 7019.0 and 14035.6 are related to +2 and +1 ions corresponding to the full length TTR monomer. The mass of recombinant V122I TTR includes the additional N-terminal glycine, alanine and methionine residues indicated as G (-2), A (-1) and M (0) respectively.

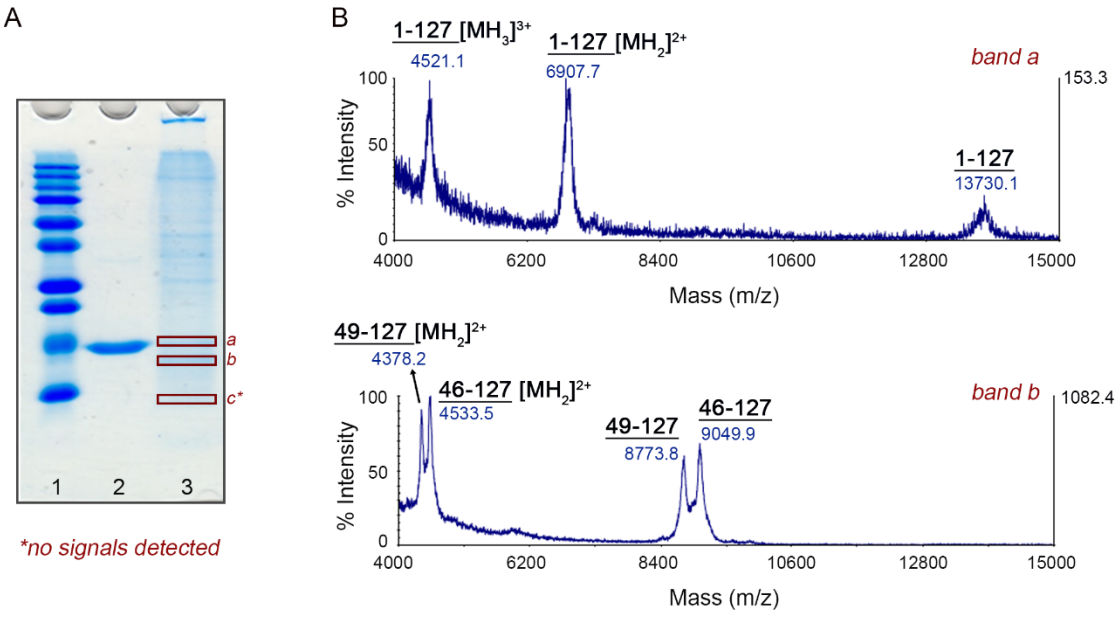


**Fig. S3. Main component in the V122I ATTR fibrils.** *A*, SDS 15% PAGE under reducing conditions of V122I ATTR fibrils. Lane 1, marker proteins (250, 150, 100, 75, 50, 37, 25, 20, 15 and 10 kDa respectively); lane 2, recombinant V122I TTR (2.5 µg); lane 3, *ex vivo* amyloid fibrils from the heart of a V122I ATTR patient (40 µg). Bands *a*, *b* and *c* were passively eluted for identification. *B*, MALDI TOF spectra of electrophoretic eluted bands acquired in linear mode. Spectrum of *band a* shows peaks at 4521.1, 6907.7 and 13730.1 corresponding to +3, +2 and +1 ions of the full length TTR monomer. MALDI TOF spectrum of *band b* shows peaks of +2 and +1 ions corresponding to the 49-127 and 46-127 TTR fragments. Material eluted off the *band c* consistent with the apparent size of the 81-127 TTR fragment did not show any detectable peak.
All protein/peptide identified contained both wild type and V122I TTR isoforms as shown with further digestions with trypsin or AspN proteases (data not shown).