

WHAT IS CLAIMED IS:

1. A method of detecting misfolded transthyretin (TTR) in a biological sample, the method comprising:

(a) contacting a biological sample with a capture antibody that specifically binds to an epitope within residues 89-97 of TTR, wherein the capture antibody comprises three Kabat heavy chain CDRs, CDR-H1 of SEQ ID NO:75, CDR-H2 of SEQ ID NO:76, and CDR-H3 of SEQ ID NO:77, and three Kabat light chain CDRs, CDR-L1 of SEQ ID NO:78, CDR-L2 of SEQ ID NO:79, and CDR-L3 of SEQ ID NO:80, and a reporter antibody that specifically binds to a different epitope of TTR; wherein if misfolded TTR is present in the sample, the capture antibody and reporter antibody bind to the misfolded TTR forming a sandwich complex, wherein the biological sample is a plasma sample from a hereditary ATTR patient carrying a E89K or E89Q mutation in the amino acid sequence of TTR; and

(b) detecting the reporter antibody that forms a sandwich complex in step (a), if any, to indicate presence or absence of the misfolded TTR.

2. The method of claim 1, wherein the capture antibody is 9D5.

3. The method of any of claims 1-2, wherein the reporter antibody is 18C5, 8C3, 7G7, AD7F6, RT24, NI-301.35G11, MFD101, MDF102, MFD103, MFD105, MFD107, MFD108, MFD109, MFD111, MFD114, or a chimeric version or humanized version thereof or a polyclonal anti-TTR antibody.

4. The method of any one of claims 1-2, wherein the reporter antibody is an antibody that binds within residues 101-109, 118-122, 115-124, 53-63, 54-61, 36-49, 49-61, 109-121, 30-66, 70-127, 80-127, 90-127, 100-127, 110-127, or 115-127 of TTR.

5. The method of any preceding claim, wherein the misfolded TTR includes an E89K substitution or an E89Q substitution.

6. The method of any one of claims 1-5, wherein the biological sample is a first aliquot of a collected sample and the method further comprises repeating step (a) and (b) on

a second aliquot of the collected sample further comprising a test antibody that competes with the capture antibody for binding to TTR.

7. The method of claim 6, wherein the test antibody is 14G8 or a chimeric or humanized form thereof, the capture antibody is 9D5, and the reporter antibody is a polyclonal anti-TTR antibody.

8. The method of any preceding claim, wherein the reporter antibody has an electrochemiluminescent label and is detected by electrochemiluminescence.

9. The method of any preceding claim, wherein the capture antibody has a biotin label.

10. The method of any preceding claim, wherein the capture antibody is bound to a solid phase before the contacting step.

11. The method of claim 10, wherein the capture antibody is attached to the solid phase via a linker.

12. The method of claim 10, wherein the solid phase comprises at least one electrode.

13. The method of any preceding claim, wherein the biological sample is from a patient receiving treatment for a transthyretin-mediated amyloidosis.