Claims

1. A human-derived anti-transthyretin (TTR) antibody or an antigen-binding fragment thereof, which is capable of binding mutated, misfolded, misassembled and/or aggregated TTR species and/or fragments thereof and does not substantially recognize physiological TTR species, wherein the antibody or antigen-binding fragment thereof comprises in its variable region or binding domain

   (a) the complementarity determining regions (CDRs) of the V_H and/or V_L variable region amino acid sequence depicted in any one of Figs. 1A to 1T, wherein one or more of the CDRs may comprise one or two amino acid substitutions, or

   (b) an amino acid sequence of the V_H and/or V_L region as depicted in any one of Figs. 1A to 1T, wherein the V_H and/or V_L region may comprise one or more amino acid substitutions.

2. The antibody of claim 1, wherein the antibody is capable of binding

   (i) a TTR epitope which comprises or consists of the amino acid sequence EEEFVEGIY (SEQ ID NO: 49), GELHGLTTEEE (SEQ ID NO: 50), or WEPFA (SEQ ID NO: 51), and/or

   (ii) a non-linear, conformational epitope.

3. The antibody of claim 2, wherein the antibody binds the TTR epitope (i) GELHGLTTEEE (SEQ ID NO: 50) but not a corresponding L55P mutant epitope or (ii) WEPFA (SEQ ID NO: 51) but not a corresponding E42G mutant.

4. The antibody of any one of claims 1 to 3, wherein the antibody or antigen binding fragment thereof further comprises a constant domain.

5. The antibody of claim 4, wherein the constant domain is a human constant domain, preferably of the IgG type, most preferably of the IgG1 class or isotype.

6. The antibody of any one of claims 1 to 5, which is a chimeric murine-human or a murinized antibody.

7. The antibody of any one of claims 1 to 6, which is an antibody fragment selected from the group consisting of a single chain Fv fragment (scFv), an F(ab') fragment, an F(ab) fragment, and an $F(ab')_2$ fragment.

8. A polynucleotide or polynucleotides encoding the antibody of any one of claims 1 to 7, preferably wherein the polynucleotide is a cDNA.

9. A vector or vectors comprising the polynucleotide(s) of claim 8.

10. A host cell comprising the polynucleotide(s) of claim 8 or the vector(s) of claim 9.

11. Use of the polynucleotide(s) of claim 8, the vector(s) of claim 9, or the host cell of claim 10 for the production of an anti-TTR antibody.

12. A method for preparing an anti-TTR antibody, said method comprising
    (a) culturing the cell of claim 10; and
    (b) isolating the antibody from the culture.

13. An antibody encoded by the polynucleotide(s) of claim 8 or obtainable by the method of claim 12.

14. The antibody of any one of claims 1 to 7 or 13, which
    (i) comprises a detectable label, preferably wherein the detectable label is selected from the group consisting of an enzyme, a radioisotope, a fluorophore and a heavy metal; and/or
    (ii) is attached to a drug.

15. A peptide having an epitope of TTR specifically recognized by an antibody of any one of claims 1 to 7, 13 or 14, preferably wherein the peptide comprises an amino acid sequence as defined in claim 2 or a modified sequence thereof in which one or more amino acids are substituted, deleted and/or added, wherein the peptide is recognized by the antibody of any one of claims 1 to 3, preferably wherein the peptide is an antigen.

16. A composition comprising the antibody of any one of claims 1 to 7, 13 or 14, the polynucleotide(s) of claim 8, the vector(s) of claim 9, the cell of claim 10 or the peptide of claim 15, preferably wherein the composition

(i) is a pharmaceutical composition comprising the antibody of any one of claims 1 to 7, 13 or 14, the cell of claim 10 or the peptide of claim 15 and further comprises a pharmaceutically acceptable carrier, preferably wherein the composition is a vaccine and/or comprises an additional agent useful for preventing or treating diseases associated with TTR amyloidosis; or

(ii) a diagnostic composition comprising the antibody of any one of claims 1 to 7, 13 or 14, the cell of claim 10 or the peptide of claim 15, preferably further comprising reagents conventionally used in immuno or nucleic acid based diagnostic methods.

17. An anti-TTR antibody or a TTR-binding fragment of any one of claims 1 to 7, 13 or 14 having substantially the same binding specificities of any one thereof, the polynucleotide(s) of claim 8, the vector(s) of claim 9, the cell of claim 10, the peptide of claim 15 or the composition of claim 16 for use in the prophylactic or therapeutic treatment of a disease associated with TTR amyloidosis, preferably wherein the disease is selected from the group consisting of Familial Amyloid Polyneuropathy (FAP), Familial Amyloid Cardiomyopathy (FAC), Senile Systemic Amyloidosis (SSA), systemic familial amyloidosis, leptomeningeal / Central Nervous System (CNS) amyloidosis including Alzheimer disease, TTR-related ocular amyloidosis, TTR-related renal amyloidosis, TTR-related hyperthyroxinemia, TTR-related ligament amyloidosis including carpal tunnel syndrome, rotator cuff tears and lumbar spinal stenosis, and preeclampsia.

18. The antibody of any one of claims 1 to 7, 13 or 14 for use in *in vivo* detection or imaging of or targeting a therapeutic and/or diagnostic agent to TTR in the human or animal body, preferably wherein said *in vivo* imaging comprises scintigraphy, positron emission tomography (PET), single photon emission tomography (SPECT), near infrared (NIR), optical imaging or magnetic resonance imaging (MRI).

19. An *in vitro* method for diagnosing a disorder associated with TTR amyloidosis, comprising steps of determining the presence of an antibody that binds to a peptide of claim 15 in a biological sample of said subject.

20. A kit useful in the diagnosis or monitoring of a disorder associated with TTR amyloidosis, said kit comprising at least one antibody of any one of claims 1 to 7, 13 or 14 or a TTR binding molecule having substantially the same binding specificities of any one thereof, the polynucleotide(s) of claim 8, the vector(s) of claim 9 or the cell of claim 10 and/or the peptide of claim 15, optionally with reagents and/or instructions for use.

21. A method of diagnosing a disease associated with TTR amyloidosis as defined in claim 17, monitoring the treatment of the disease with an anti-TTR antibody or determining the diagnostic or therapeutic utility of an anti-TTR antibody comprising assaying the level of misfolded and/or aggregated TTR in a sample of a body fluid from a subject following administration of an anti-TTR antibody to the subject, wherein the presence or elevated level of misfolded and/or aggregated TTR in the sample of the subject compared to a control indicates a disease associated with TTR amyloidosis.

22. The method of claim 21, wherein the level of misfolded and/or aggregated TTR in the sample is assayed by determining a complex formed between the anti-TTR antibody and the misfolded and/or aggregated TTR.

23. The method of claim 21 or 22, wherein the control is a sample obtained from the subject prior to administration of the anti-TTR antibody.

24. The method of any one of claims 21 to 23, wherein the body fluid is blood and the sample is derived thereof and/or the control is a corresponding sample of a body fluid taken from the subject prior to administration of the anti-TTR antibody.

25. The method of any one of claims 21 to 24, wherein the subject is a non-human animal or a human.

26. The method of any one of claims 21 to 25, wherein the anti-TTR antibody is an anti-TTR antibody or antigen-binding fragment of any one of claims 1 to 7, 13 or 14.

27. Use of an anti-TTR antibody in the method of any one of claims 21 to 26, preferably wherein the antibody is an anti-TTR antibody or antigen-binding fragment of any one of claims 1 to 7, 13 or 14.