CLAIMS

1. A method for identifying a subject as a candidate for further diagnostic testing and/or a therapeutic intervention for an amyloidosis disorder, the method comprising:

(a) detecting an ApoE peptide and measuring the concentration of Aβ42 and Aβ40 and optionally a marker of neurodegeneration in a blood sample obtained from the subject in a single assay using immunoprecipitation and mass spectrometry (IP/MS), and then determining ApoE ε4 status, wherein the ApoE e4 status is the presence of epsilon 4 allele on an apolipoprotein E gene, calculating the Aβ42/Aβ40 value and optionally determining the concentration of the marker of neurodegeneration; and

(b) identifying the subject as a candidate for further diagnostic testing and/or a therapeutic intervention for the amyloidosis disorder when the subject is an ApoE ε4 carrier and the Aβ42/Aβ40 value is less than 0.126, and identifying the subject as not a candidate for further diagnostic testing or therapeutic intervention when the subject is not an ApoE ε4 carrier and the Aβ42/Aβ40 value is greater than 0.126~~the Aβ42/Aβ40 value is obtained by a system that provides a probability of detecting Aβ amyloidosis equal to or greater than about 90%~~.

2. A method for detecting Aβ amyloidosis, the method comprising:

(a) detecting an ApoE peptide and measuring the concentration of Aβ42 and Aβ40 and optionally a marker of neurodegeneration in a blood sample obtained from the subject in a single assay and mass spectrometry (IP/MS), and then determining ApoE ε4 status, wherein the ApoE e4 status is the presence of epsilon 4 allele on an apolipoprotein E gene, calculating the Aβ42/Aβ40 value and optionally determining the concentration of the marker of neurodegeneration; and

(b) identifying the subject as having or at risk of developing Aβ amyloidosis when the subject is an ApoE ε4 carrier and the Aβ42/Aβ40 value is less than 0.126, and identifying the subject as not having or being at risk of

developing Aβ amyloidosis when the subject is not an ApoE ε4 carrier and the Aβ42/Aβ40 value is greater than 0.126~~the Aβ42/Aβ40 value is obtained by a system that provides a probability of detecting Aβ amyloidosis equal to or greater than about 90%~~.

3. A method for grading a subject for ~~the~~ a stage of ~~disease~~an amyloidosis disorder, the method comprising:

(a) detecting an ApoE peptide and measuring the concentration of Aβ42 and Aβ40 and optionally a marker of neurodegeneration in a blood sample obtained from the subject in a single assay and mass spectrometry (IP/MS), and then determining ApoE ε4 status, wherein the ApoE e4 status is the presence of epsilon 4 allele on an apolipoprotein E gene, calculating the Aβ42/Aβ40 value and optionally determining the concentration of the marker of neurodegeneration; and

(b) identifying the subject as having or at risk of developing ~~disease~~ the amyloidosis disorder when the subject is an ApoE ε4 carrier and the Aβ42/Aβ40 value is less than 0.126, and identifying the subject as not having or being at risk of developing the amyloidosis disorder when the subject is not an ApoE ε4 carrier and the Aβ42/Aβ40 value is greater than 0.126~~the Aβ42/Aβ40 value is obtained by a system that provides a probability of detecting disease equal to or greater than about 90%~~.

4. A method of selecting subjects for a clinical trial for treating Aβ amyloidosis, the method comprising:

(a) detecting an ApoE peptide and measuring the concentration of Aβ42 and Aβ40 and optionally a marker of neurodegeneration in a blood sample obtained from the subject in a single assay and mass spectrometry (IP/MS), and then determining ApoE ε4 status, wherein the ApoE e4 status is the presence of epsilon 4 allele on an apolipoprotein E gene, calculating the Aβ42/Aβ40 value and optionally determining the concentration of the marker of neurodegeneration; and

(b) identifying the subject as a candidate for the clinical trial when the subject is an ApoE ε4 carrier and the Aβ42/Aβ40 value is less than 0.126, and identifying the subject as not a candidate for the clinical trial when the subject is not an ApoE ε4 carrier and the Aβ42/Aβ40 value is greater than 0.126~~the Aβ42/Aβ40 value is obtained by a system that provides a probability of detecting Aβ amyloidosis equal to or greater than about 90%~~.

5. The method of any one of the preceding claims, wherein the Aβ42/Aβ40 value is about 0.125 or less.

6. The method of any one of the preceding claims, wherein the Aβ42/Aβ40 value is about 0.124 or less.

7. The method of any one of the preceding claims, wherein the probability of diagnosing the disease is calculated using a receiver operating curve (ROC) area under the curve (AUC).

8. The method of any one of the preceding claims, wherein ~~the~~ a predetermined threshold is determined by a data point of the highest specificity at the highest sensitivity on the ROC curve.

9. The method of any one of the preceding claims, wherein the marker of neurodegeneration is selected from one or more of neurofilament light chain, tau isoforms, visinin-like protein 1, and neurogranin isoforms.

10. The method of any one of the preceding claims, wherein the subject (a) was not previously diagnosed with Aβ amyloidosis, (b) is asymptomatic, (c) is a potential participant in a clinical trial for a disease associated with Aβ amyloidosis, (d) is a candidate for amyloid imaging, or (e) any combination of (a) through (d).

11. The method of claim 3 further comprising determining a treatment to be administered based on the grade of Aβ amyloidosis.

12. The method of claim 11, wherein the treatment to be administered is a non-pharmacological treatment, a pharmacological treatment, or treatment with an imaging agent followed by detection of the imaging agent.

13. The method of claim 12, wherein the imaging agent is a functional imaging agent or a molecular imaging agent.

14. The method of claim 11, wherein the treatment to be administered is a non-pharmacological treatment.

15. The method of claim 11, wherein the treatment to be administered is a pharmacological treatment.

16. The method of claim 11, wherein the treatment to be administered is administered through a clinical trial.

17. A functional imaging agent or a molecular imaging agent for use in a method of treating a subject with Aβ amyloidosis, the method comprising:

(a) detecting an ApoE peptide and measuring the concentration of Aβ42 and Aβ40 and optionally a marker of neurodegeneration in a blood sample obtained from the subject, and then determining ApoE e4 status, calculating the Aβ42/Aβ40 value and optionally determining the concentration of the marker of neurodegeneration; and

(b) identifying a subject for treatment when the subject is not an ApoE ε4 carrier and the Aβ42/Aβ40 value is less than 0.126, and not treating the subject when the subject is not an ApoE ε4 carrier and the Aβ42/Aβ40 value is greater than 0.126~~the Aβ42/Aβ40 value is obtained by a system that provides a probability of detecting Aβ amyloidosis equal to or greater than about 90%~~.

18. Use of a functional imaging agent or a molecular imaging agent in the manufacture of a medicament for a method of treating a subject with Aβ amyloidosis, the method comprising:

(a) detecting an ApoE peptide and measuring the concentration of Aβ42 and Aβ40 and optionally a marker of neurodegeneration in a blood sample obtained from the subject, and then determining ApoE e4 status, calculating the Aβ42/Aβ40 value and optionally determining the concentration of the marker of neurodegeneration; and

(b) identifying a subject for treatment when the Aβ42/Aβ40 value is less than 0.126, and not treating the subject when the subject is not an ApoE ε4 carrier and the Aβ42/Aβ40 value is greater than 0.126~~the Aβ42/Aβ40 value is obtained by a system that provides a probability of detecting Aβ amyloidosis equal to or greater than about 90%~~.